Applicability and effectiveness of the Dutch Multidisciplinary Guidelines for the treatment of Anxiety Disorders in everyday clinical practice

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'De toepasbaarheid en effectiviteit van de Nederlandse multidisciplinaire richtlijnen voor de behandeling van angststoornissen in de dagelijkse klinische praktijk' (met een samenvatting in het Nederlands)

Maarten Kornelis van Dijk

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Contents

CHAPTER 1

General introduction

1.1. Introduction

In 2001 the Institute of Medicine (IOM) published an alarming report on the quality of healthcare in the United States, titled 'crossing the quality chasm: a new health system for the 21st century' [1]. This report suggested that the American healthcare system faced major challenges on the aspects of improving patient-centeredness, improving patient safety and putting scientific knowledge into practice. It stated that especially because of the continuing stream of technological and scientific developments, there was not only a gap between the optimal quality of care and the current healthcare practices of that time, but actually a chasm. A subsequent report that focused on healthcare for mental and substance abuse conditions in America, suggested that the quality of care for patients suffering from these conditions needed improvement too. This report explicitly stated that there was a discrepancy in care that is known to be effective and the care that is actually delivered in mental healthcare [2].

The above mentioned IOM reports on the quality of healthcare in the United States received much attention worldwide. In many governments and international governmental bodies the IOM reports sparked an interest in issues regarding the quality of healthcare, since the failing standard of healthcare are not limited to the USA but hold for many other Western countries as well. For instance Kelley & Tucci in their article in the British Medical Journal wrote that the key message of the alarming IOM report would probably be considered "old news" by the public and many healthcare providers [3], thereby providing input to the idea that at least the healthcare system in the UK was confronted with the same issues. In 2005 the Dutch National Board for Healthcare came to the same conclusions about the quality of the healthcare system in the Netherlands, especially the speed at which effective treatments found their way into daily clinical practice was considered far too slow. Consequently possible health gains that could be achieved with the proper implementation of these evidence-based interventions could not be reached. Moreover, the wellbeing of

the healthcare consumers would fall short of expectations resulting in a unnecessarily high financial burden because of the provision of suboptimal care [4].

When we consider the existing research on adequacy of care for anxiety and depressive disorders at the time of the IOM reports the picture emerges of failing standards of quality of care. The U.S. National Comorbidity Survey Replication study that was carried out between 2001 and 2003 in the United States, reported that in primary care, no more than 14% of the patients with anxiety disorders or depressive disorders received adequate treatment. In secondary care, only a little over 50% of the patients with an anxiety or depressive disorder in secondary mental healthcare received adequate treatment [5]. During the same time period, the situation in Europe was not much better. The ESEMeD study that was carried out among the general population of six Western European countries, including the Netherlands, showed that in primary care only 23% of the patients with anxiety or depressive disorders received adequate treatment. According to the same study, in secondary mental healthcare 57% of the patients with an anxiety or depressive disorder were adequately treated [6]. These figures give quite a sad picture of the quality of mental healthcare at that time, certainly when one realizes that only minimal criteria for determining adequacy of care were used. A patient was judged to have received adequate treatment, if he/she reported receiving either: antidepressant medication (for depressive disorder) or antidepressants or anxiolytic drugs (for anxiety disorders) for at least 2 months plus at least four visits with a psychiatrist, a GP or any other doctor; or at least eight sessions of talking therapy with a psychologist or a psychiatrist lasting an average of 30 minutes [5, 6]. This means that details on the type and dosage of the prescribed antidepressant or anxiolytic medication were not taken into account nor information about the type of psychotherapeutic treatment.

An important reaction to the slow adoption of evidence-based treatment interventions in daily clinical practice was the large-scale development of clinical practice guidelines. Clinical practice guidelines have been defined by the Institute of Medicine as "systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances" [7; page 38]. In most cases "systematic development" includes the comprehensive and rigorous evaluation of scientific and clinical evidence according to explicitly stated norms. The aim of publishing these guidelines was to increase knowledge about scientific evidence for specific practices, thereby hoping that evidence-based treatments would be adopted on a larger scale in clinical practice. Furthermore, the expectation was that successful

implementation of such guidelines would reduce unwanted variation in healthcare practices and improve the quality of care. Other fields of medicine have a longer tradition of producing guidelines for clinical practice. Over the last two decades the development of treatment guidelines in mental healthcare also expanded and continuous to expand.

1.2. Clinical Practice Guidelines in Mental Healthcare

The development and dissemination of guidelines in Mental Health started in the US in the early nineties of the former century and in the Netherlands about 10 years later. The first guidelines were mono-disciplinary and focused primarily on pharmacotherapeutic treatment. In the late 1990s the UK also started with the development and dissemination of guidelines for psychologists and psychotherapists [8]. The precursor to UK guidelines for psychologists and psychotherapists was a strategic review of policy on psychotherapy services published by the Department of Health in 1996. The rationale for developing these guidelines for psychologists was to ensure a proper place for psychological therapies in the treatment of mental conditions, besides the different available evidence-based pharmacotherapeutical treatment options. Another important goal was to promote the actual use of empirically supported psychological therapies [8].

By order of the Ministry of Health, Welfare and Sports in the Netherlands a National Steering Group for Multidisciplinary Guideline Development in Mental Health (NSGMH) and the Trimbos-institute delivered 15 guidelines for Mental Health between the period of 2003 and 2013 and even more are being developed [9]. At the beginning of this century the process of guideline development that was followed in the Netherlands was unique. From the start, the guidelines were to be multidisciplinary. The ambitious goal was to make sure that they would ultimately reflect the consensus of *all* different professional groups involved in the care for the particular condition. In addition to this it was explicitly stated they should also adequately incorporate the patient perspective. Delegates of all professional groups and patient organizations where involved in the process of developing these guidelines, ensuring broad support of all parties involved and thus promoting their actual use in daily clinical practice.

The NSGMH also made great efforts to promote the use of the guidelines in the Netherlands. A lot was done to ensure that general practitioners and

professionals working in the field of mental healthcare became acquainted with these new guidelines. Particularly the first guidelines on anxiety disorders and depressive disorders received attention in the media, and a broad outline of these guidelines was presented in Dutch scientific journals for psychiatrists and psychologists. Furthermore a website (www.ggzrichtlijnen.nl) served as a free database for professionals and patients, and presented the scientific background, recommendations and algorithms of the 15 guidelines that were published. The guidelines were sold as printed booklets by the Trimbos-institute and were freely available to be downloaded from the website of the Dutch Institute for Healthcare Improvement CBO (www.cbo.nl) and the websites of professional societies such as the Netherlands Psychiatric Association (Nederlandse Vereniging voor Psychiatrie) (www.nvvp.net). Other platforms such as conventions and educational programmes were also used to raise awareness among clinicians about the launch of the guidelines [10].

Despite all efforts in the Netherlands, the multidisciplinary guidelines for mental healthcare were not received well by all professionals. Fundamental points of critique were: the DSM-IV classification as a starting point for development of the guidelines [11] and the medical perspective with a primary focus on symptom reduction. Some non-medical professions considered the focus of the guidelines to be too narrow [12, 13]. Another point of critique formed the importance of scientific evidence as the primary selection criterion for the treatment interventions included in the guidelines. This selection criterion strongly favoured treatments investigated in randomized controlled trials (RCTs), while less thoroughly investigated forms of treatment were excluded from these guidelines. This practice sometimes contrasted experiences of healthcare providers in the field, who regarded these treatments to be valuable. [12, 13, 14]. Finally, many healthcare providers doubted the applicability of the guideline recommendations in clinical practice, because of the suspected bias of the research populations used in RCTs.

Despite all the efforts made by the NSGMH to promote guideline adherence, daily clinical practice showed to be very unruly. A survey on the use of national guidelines developed for mental healthcare, conducted among a representative sample of 406 Dutch mental healthcare professionals in 2009, showed that although 91% of these professionals reported being familiar with these guidelines, only 28% said that they actually used them [12]. The implementation of guidelines appeared to be a challenging task. An important question remained whether the development and implementation of these guidelines is worth the effort.

1.3. Effectiveness of adhering to mental health guidelines

The successful implementation of mental health practice guidelines is expected to improve the quality of care by promoting the use of 'evidence-based' practices. At the time of completing the first draft of the research proposal that formed the basis for this thesis, there was little research to support the claim that adherence to guidelines would yield superior results compared with "treatments as usual". Now, a decade later, this evidence is still largely absent. Very few evaluations have been made. This is rather strange, if one takes into account the enormous amounts of money and efforts that have been put in developing the guidelines.

Indirect evidence for improved quality of care if all patients receive 'evidence-based' treatments is however provided by a publication of Andrews and colleagues [15]. Andrews and colleagues used epidemiological data from the 'Australian National Survey of Mental Health and Wellbeing', to calculate the number of years lived in disability (YLDs) that was averted by Australian healthcare system for mentally ill patients [15]. This given the actual treatments for ten different mental disorders as offered at that time. Based on estimates of the effectiveness of available evidence-based treatment interventions for these ten mental disorders, averted YLDs of the hypothetical scenario that these same patients would only receive optimal care, according to the principles of evidence-based medicine at the same coverage, was also calculated. Furthermore, the same calculations were performed for the scenario that this type of optimal care was provided at 100% coverage. Additionally, for all three scenarios the direct treatment costs were calculated, so as to be able to obtain a cost-effectiveness estimate in Australian dollars per YLD. Summarizing the final results for the total group of mental disorders, the authors concluded that, compared to current treatments, the scenario of provision of optimal treatments would avert a greater proportion of the burden of mental disorders without higher costs, even when taking into account the fact that optimal care was more comprehensive. According to the authors, optimal care would result in lower costs due to fewer in-patient stays. Furthermore it was presumed that the health expenses would be limited because costly treatments that are not expected to generate any benefit would no longer be used [15].

It was established that in Australia 1 086 331 people suffered from an anxiety disorder at the time of the survey. This group of people counted for a total of 201 547 YLDs. With the practices used at that time, the Australian healthcare was able to avert a little over 26 000 YLDs for this group of patients. According

to the estimations of the authors, this figure could beat least 40 000 YLDSs if the same patients that now received treatment would only be given an evidence-based form of treatment [15].

The conclusions of the above-mentioned study, however, were based on modelled scenarios. Because of the theoretical nature of the study, quite a large number of assumptions were made. For instance, from the publications it appears that in identifying the YLDs averted with the mix of healthcare services provided to the prevalent cases, only information on the effect-sizes of evidence-based treatments were used. The assumption was that non-evidence-based treatments included in this mix did not have any effect at all because of a lack of scientific evidence. As a result the found increase in averted YLDs in the study, for the scenario that only evidence-based treatments would be provided, may actually have been overestimated.

Statements about improved effectiveness when implementing 'evidence-based' interventions in daily clinical practice, really requires research in which direct comparisons are made between the treatment results obtained through usual care and the treatment results obtained when optimal care is provided according to the principles of evidence-based medicine.

A publication of Bauer that was published in 2002 sheds further light on the effectiveness of guidelines [16]. Bauer provided the first overview of quantitative studies evaluating outcome and treatment adherence to Mental Health Clinical Practice Guidelines that were published before the year 2000. His literature search yielded 41 studies. These studies can be subdivided into three categories: 26 were cross-sectional investigations performed after the release of guidelines, 6 were conducted before and after release of guidelines without a specific intervention and 9 involved a controlled trial of a specific implementation intervention. The investigated guidelines dealt with a diverse set of topics, ranging from antipsychotic use, smoking cessation, and the treatment of specific mental conditions such schizophrenia and bipolar disorders. Most studies did however investigate adherence to guidelines specific for the treatment of depression. Only 15 (37%) of the studies identified by Bauer were conducted in the mental health specialty sector. Adequate adherence was found in 27% of the cross-sectional and the pre-post studies versus 67% of the controlled trials. In only 13 of the 41 studies included, data on treatment outcome had been collected as well as data on guideline adherence. In only 6 of these 13 studies (46%), greater guideline adherence was actually associated with better treatment results.

Weinmann and colleagues in 2007 published a review that included only comparative studies on the effects of psychiatric guideline implementation on

provider performance and treatment outcome only [17]. They identified 18 studies (9 randomized-controlled trials, 6 nonrandomized-controlled studies and 3 quasi experimental pre-post studies) published between 1966 and 2006. Most studies included focused on the guidelines for depressive disorder. Other studies dealt with guidelines for schizophrenia, bipolar disorder, delirium or dementia and smoking cessation. The review showed that effects of guideline implementation on provider performance or patient outcomes were moderate at best and of temporary duration in most cases. It was also found that the implementation of guidelines can have a negative effect on treatment outcome, as was the case in one study that focused on prescribing antidepressant medication in primary care for patients with depressive disorder [18]. The authors of this study suggest that the negative effect on the functional status of the patients might be due to the chronicity of depressive symptoms of the patient group under study. In addition, the authors suggest that new research and special guidelines are needed to improve the treatment of patients suffering from chronic or recurring major depressive disorder [18].

So far, the results on the effectiveness of implementing guidelines do not look convincing. Weinmann and colleagues suggested however, that the type of diagnosis could critically influence the magnitude of treatment outcome obtained by successful implementation of guidelines [17]. In contrast to severe mental illness (SMI), such as schizophrenia and dementia, (non-chronic) depressive disorders could be a more favourable area of mental healthcare for improving outcomes through the implementation of guidelines [17]. According to the authors, the treatment of SMI could be more complex than that of depressive disorders, and thus, improving treatment outcome for SMI might be more difficult to achieve [17].

Since the publication of the reviews of Bauer and Weinmann and colleagues at least three more studies have confirmed the positive effects of implementing treatment guidelines for depressive disorders [19, 20, 21]. In the first of these studies, depressed inpatients were randomized to either an algorithm-guided standardized stepwise drug treatment regimen or treatment as usual (TAU). The probability of remission was found to be higher in patients receiving care according to the medication algorithm. In the condition in which the algorithm was followed, the average time to remission was 5 weeks shorter [19]. The second study that evaluated another medication algorithm, found a higher remission rate (60.2%) in depressed outpatients who were randomized to an algorithm of guided treatment (AGT) vs. treatment as usual (TAU) (49.7%). The median number of days to achieve remission in the AGT group (93 days)

was half as long as that in the TAU group (191 days) [20].The third study evaluated the systematic implementation of guidelines for depression and suïcidality in 6 psychiatric clinics, of which two served as controls. Guideline adherence was found to be higher in the clinics in which the guidelines were systematically implemented and not only disseminated. Furthermore, patients treated in clinics in which the guidelines were systematically implemented, showed greater treatment gains at lower cost compared to patients treated in the control clinics [21].

These studies [19, 20, 21] provide evidence that implementing guidelines is an endeavour worth pursuing, at least in affective disorders. Findings such as these also warrant additional research into the effectiveness of implementing guidelines for other common mental disorder for which potent evidence-based treatment options exist. This thesis will focus on such an endeavour in the treatment of patients with an anxiety disorder. It was, however, stated that the evidence of the effects of a specific guideline could not be separated from the evidence concerning the effectiveness of specific implementation strategies [17]. The important question which implementation strategies are effective will be addressed in this thesis as well.

1.4. Implementation strategies

The review of Bauer [16] included several studies in which guideline adherence levels were compared before and after publication of guidelines without further intervention. Results of these studies in terms of changing provider behaviour were generally poor. The results suggest that if one aims to implement guidelines, active intervention is necessary. Both reviews [16, 17] conclude that it is not possible yet to identify one single strategy for guideline implementation that is most effective. However, studies that reported positive outcomes were found to have used so-called “complex multifaceted interventions”, or certain psychological methods that are used to overcome specific barriers to change in the process of guideline implementation.

Certainly at the time of the publication of these two reviews, no “ready-made” implementation strategy could be viewed as superior for mental healthcare in all types of situations. The same held for changes in the somatic healthcare system [22]. The use of a tailor-made implementation program is therefore suggested [22], matching the specific setting and needs of the target group among which changed behaviour is sought. Developing such a tailor-made

implementation program seemed to be a promising strategy when implementing guidelines for anxiety disorders too. Since studies focusing on the implementation of guidelines for anxiety disorders had never been performed, we thereby also wanted to study the feasibility of implementing these guidelines when using such a tailor-made implementation approach.

1.5. Anxiety disorders and the use of practice guidelines

Anxiety disorders cover a phenomenological diverse group of mental disorders that share a core feature of excessive or unreasonable anxiety and/or fear experienced by the patient. The various anxiety disorders differ in focus and pattern of anxiety, the avoidance of feared situations and the presence of specific symptoms like excessive worrying or obsessive behaviour.

In the Netherlands about 1.3 million people suffer from an anxiety disorder [23]. Anxiety disorders are known to markedly compromise quality-of-life and psychosocial functioning in several functional domains [24]. Anxiety disorders, with a lifetime prevalence of 19.6% as a group, belong to the most prevalent mental disorders in the Netherlands. Being surpassed only slightly by the mood disorders, for which a life-time prevalence of 20.2% was found. The lifetime prevalence of anxiety disorders appears to have been quite stable during the last decennium [25]. It is estimated that each year about 180 million Euros are spent on healthcare for patients suffering from anxiety disorders in the Netherlands [23]. However, the indirect costs to society have been estimated much higher. Untreated anxiety disorders mostly run a chronic course [26], resulting in an increased non-psychiatric medical consumption and ongoing costs due to absenteeism and loss of productivity at work [27].

The ESEMeD study [6] showed that, compared with 5 other European countries, the Netherlands performed best with an overall proportion of 55.4% adequate care for depressive or anxiety disorder patients. This proportion is still rather low, especially when you consider that only minimal criteria for judging adequacy of care were used (the prescription of antidepressant of anxiolytic medication, or having had 8 contacts with a psychiatrist or psychologist for psychotherapeutic treatment). Such an estimation is considered far too low, because 8 sessions of psychotherapeutic treatment does not necessarily mean that the psychotherapeutic care has been optimal. Research carried out in the Netherlands around 2000 showed that although about 90% of anxiety disorder patients treated in the Netherlands were offered some form of psychotherapy,

only one third of them actually received an evidence based form of psychotherapy in the form of directive therapy [28].

A more recent cross-sectional study performed by Bet and colleagues (2013) showed that these figures on adequacy of care have only improved very little over the years [29] even despite the publication of the Dutch multidisciplinary guidelines for mental healthcare. This study used the baseline measurement data from the NESDA study [30] to assess treatment inadequacy in primary and secondary care in patients suffering from major depressive disorder (MDD) or an anxiety disorder (n=1662). For the anxiety disorders patients with a panic disorder with or without agoraphobia, social anxiety disorder or generalized anxiety disorder were included. Adequacy of care was judged according to the recommendations of the guidelines. In case of pharmacotherapy not only the right type of medication, but also the right type of medicine that was prescribed, and adequate medication usage were assessed. In judging adequacy of psychological treatment a very rough estimate was used. A patient was considered to have received adequate psychological treatment if the patient had at least had 5 visits to a professional for 'conversations about causes of and dealing with emotional problems' in the last 6 months. This professional could be a psychiatrist, psychotherapist, trained psychologist, but also a trained social worker or social psychiatric nurse. It was found that in subjects with moderate to severe anxiety disorder (without a comorbid depressive disorders), overall only 56% of the subjects were treated sufficiently with antidepressants, benzodiazepines or psychological treatment. Treatment inadequacy was more prominent in primary care (60%) than in specialized care (30%) [29].

All of the above mentioned findings suggest anxiety disorders to be a very relevant group with regards to improving quality of care. The systematic implementation of anxiety disorder guidelines may be a means to that end. Recent figures on quality of care suggest that the "passive" dissemination of these guidelines has little to no effect. A result that could be expected, because of the findings from Bauer's review, which suggest that often more "active" intervention is necessary to successfully implement guidelines [16]. Strong evidence regarding the feasibility and the effectiveness of implementing such guidelines is yet to be found.

1.6. Predicting non-response and persisting disability when adhering to anxiety disorder guidelines

In clinical practice it would be valuable to be able to identify risk factors for non-response to care which is delivered according to the multidisciplinary

guidelines. If these risk factors were known, the clinician would be able to make proper treatment adjustments in an early stage of treatment. An important question therefore is "if it is possible to predict in advance for which patients adhering to the anxiety disorder guideline recommendations will not be beneficial?". However, so far research has yielded few reliable predictors of treatment prognosis.

After studying the literature, Taylor and colleagues conclude that in the treatment of anxiety disorder patients, factors such as low treatment motivation, hidden secondary motives for seeking treatment, experienced barriers that hamper in attending treatment, pre-treatment symptom severity and the presence and severity of possible comorbid psychopathology could be relevant for predicting the course of treatment and treatment outcomes [31].

When looking at treatment predictors, another important long-term treatment outcome to consider might be persisting functional impairments. Especially from a societal perspective where such impairments could predict continued need for treatment and a decreased ability to participate in society. A systematic review on prognostic factors of long term disability in mental disorders performed by Cornelius et al [32] sheds light on some factors that may be of interest when studying persisting functional impairments despite provision of adequate care. In this review strong evidence was found for age as a relevant factor for continuous disability. Limited evidence was found for gender, education, unemployment, and socio-economic status.

The above-mentioned predictor variables have never been specifically studied in a treatment situation when evidence-based practice guidelines for anxiety disorders are properly delivered. The question to be answered is whether clinical risk factors may be identified which will allow to predict in advance which patients will show treatment non-response or which patients run the risk of persisting functional impairments when treated according to these guidelines.

1.7. Research questions and outline of this thesis

From the paragraphs above it can be concluded that there is a clear need to improve the quality of care for patients with an anxiety disorder. As suggested, the implementation of anxiety disorder practice guidelines may be an answer to that need. However, it remains largely unknown which implementation methods may be effective and whether the implementation of clinical guide-

lines for this group of patients is actually feasible. In addition, the question is not resolved whether successful implementation of these guidelines improves treatment outcomes. Finally, it is largely unknown whether there are any patient characteristics that could predict treatment non-response or persisting functional impairments when adhering to the guidelines. These research questions will be addressed in the following chapters 2 to 5.

Chapter 2 describes the results of a case study, in which the Dutch anxiety disorder guidelines were implemented in the community mental healthcare centre of Almelo. Changes in provider behaviour in response to guideline implementation activities, before and after the start of implementation activities were closely monitored. As described in chapter 2, the study's focus was answering the question whether the implementation of the anxiety disorder guidelines in mental healthcare was feasible and finding out which implementation strategies can prove helpful in doing so.

In chapter 3 the results of a study are presented that focused on treatment results of the cohort of anxiety disorder patients, included after the start of the implementation activities in the community centre of Almelo. At 1-year follow-up treatment results of patients whose treatment adhered to the guidelines were compared to patients whose treatment did not adhere to these guidelines, thereby answering the research question whether adherence to such guidelines yields superior results to non-adherence.

In chapter 4 the results of a study are presented in which the cohort of anxiety patients treated in the community centre of Almelo after the start of the implementation activities, was compared to a control cohort from another treatment setting in which the guidelines were only passively disseminated. For this control cohort, the data from the Netherlands Study on Depression and Anxiety (NESDA) study was used [30]. Guideline adherence rates and treatment outcome at 1- and 2- year follow-up of the two cohorts were compared.

In chapter 5 it is described how in a subsample of patients whose treatments were found to adhere to the guidelines, risk factors of non-response and persisting disability were studied as determined at 1-year follow-up. In this study many predictors of treatment outcome in anxiety disorders were included in concert.

Finally, in chapter 6 the findings of the chapters 2 to 5 will be discussed and recommendations for future research will be described.

Chapter 7 gives a summary of the complete dissertation.

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CHAPTER 2

Implementing practice guidelines for anxiety disorders in secondary mental health care: A case study

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Abstract

Background: Recent years have seen the large-scale development of clinical practice guidelines for mental disorders in several countries. In the Netherlands, more than fifteen multidisciplinary guidelines for mental health care have been developed since 2003. The first dealt with the treatment of anxiety disorders. An important question was whether it is feasible to implement these guidelines because implementing practice guidelines is often difficult. Although several implementation interventions have proven effective, there seems to be no ready-made strategy that works in all circumstances.

Case description: The Dutch multidisciplinary guidelines for anxiety disorders were implemented in a community mental health care centre, located in the east of the Netherlands. The centre provides secondary outpatient care. The unit within the centre that specializes in the treatment of anxiety disorders has 16 team members with diverse professional backgrounds. Important steps in the process of implementing the guidelines were analysing the care provided before start of the implementation to determine the goals for improvement, and analysing the context and target group for implementation. Based on these analyses, a tailor-made multifaceted implementation strategy was developed that combined the reorganization of the care process, the development of instruction materials, the organization of educational meetings and the use of continuous quality circles to improve adherence to guidelines.

*Discussion and evaluation:*Significant improvements in adherence rates were made in the aspect of care that was targeted for change. An increase was found in the number of patients being provided with recommended forms of psychotherapeutic treatment, ranging from 43% to nearly 55% ($p < 0.01$). The delivery of adequate pharmacological treatment was not explicitly targeted for change remained constant.

Conclusion: The case study presented here shows that the implementation of practice guidelines for anxiety disorders in mental health care is feasible. Based on the results of our study, the implementation model used offers a useful approach to guideline implementation. By describing the exact steps that were followed in detail and providing some of the tools that were used in the study, we hope the replication of this implementation methodology is made more practical for others in the future.

Keywords

Anxiety disorders, Practice guidelines, Implementation strategy, Tools for implementation

2.1. Background

Recent years have seen the large-scale development of clinical practice guidelines for mental disorders in several countries. Based on a systematic evaluation of the existing scientific literature, these guidelines provide recommendations for clinical practice under specific clinical circumstances. By promoting evidence-based practice, these guidelines are expected to improve the quality of care [1]. The Netherlands was among the first countries to develop guidelines for mental health care, with over fifteen different multidisciplinary guidelines published since 2003 [2]. The first guideline that was published concerned the treatment of anxiety disorders [3]. Anxiety disorders constitute a highly prevalent group of mental disorders which are known to significantly compromise quality of life [4]. Despite the availability of effective psychotherapeutic and pharmacological treatments in Western countries, a large proportion of patients with anxiety disorders still do not receive an evidence-based form of treatment [5-7]. Implementing guidelines for the treatment of anxiety disorders will change that, but to date little is known on how to achieve effective implementation.

The implementation of guidelines is often a difficult process. From other fields of medicine where there is a longer tradition of producing guidelines for clinical practice, we know that the actual use of these guidelines often lags behind their availability [8]. The same holds true within mental health care. A survey on the use of national guidelines developed for mental health care, conducted among a representative sample of 406 Dutch mental health care professionals in 2009, showed that although 91% of these professionals reported being familiar with these guidelines, only 28% said that they actually used them [9].

From the existing studies on implementing guidelines in mental health care, we know that active intervention is necessary to promote adherence to these guidelines [10]. Two meta-reviews on guideline implementation within mental health care show that studies which use complex multi-faceted interventions produce the best results [10, 11]. There is a lack of convincing evidence favouring one type of intervention or a specific combination of interventions when implementing guidelines, however. Based on studies into changing medical care within the somatic health care system, Grol and Grimshaw also conclude that no ready-made implementation strategy is superior in all situations [12]. They therefore suggest an implementation model that is to be tailor-made matching the specific setting and the needs of the target group among which

changed behaviour is sought. In our study we use such an implementation model described by Grol and Wensing [13] which, because of its global and transparent structure, offers the possibility to tailor-make the implementation strategy.

This implementation model of Grol and Wensing consists of several steps that help to plan, execute and evaluate implementation systematically. The model suggests beginning by determining the goals for improvement by analysing current practices, and then analysing the context in which a change of practice routines is expected to take place. We developed two practical tools that help to provide input for these two diagnostic steps. One is a set of process indicators to measure guideline adherence. The second is a questionnaire that helps to detect factors that can impede or promote guideline adherence. By describing these diagnostic tools in combination with the resulting interpretation of the steps in the implementation model, we hope to provide an example of a sound implementation methodology that can easily be replicated by others. In our case, following this methodology proved very useful. Implementing the multidisciplinary guidelines for anxiety disorders led to a significant increase in guideline adherence.

2.2. Case description

2.2.1. The treatment setting

The community mental health centre in which the multidisciplinary guidelines for anxiety disorders was implemented is located in the Dutch provincial town of Almelo which has around 78, 000 inhabitants. It also serves the residents from the surrounding rural area with around 60, 000 inhabitants. The centre is part of a larger mental health institution, also containing (semi-)clinical facilities, being the main provider for mental health care in the region. The community mental health centre provides outpatient care and is structured according to several disorder-specific units. After being referred to the centre by their general physician, patients undergo a standard clinical interview to determine their diagnosis. According to the primary diagnosis, patients are allocated to the appropriate disorder-specific treatment unit.

The unit responsible for treating patients with anxiety disorders consisted of 16 team members when the study began. At that time, the team included: 1 psychiatrist, 1 psychiatrist in training, 1 clinical psychologist, 1 clinical psychologist in training, 2 psychotherapists, 2 health psychologists, 3 health

psychologists in training and 1 junior psychologist waiting to start training, 3 psychiatric nurses, and 1 psychiatric nurse in training. So the team members' experience as health care professionals ranged from beginners to the very experienced. The mean age of the team members was 35 years (range 24–53).

The goals of the organization were to improve transparency and the quality of care provided by the unit for anxiety disorders by implementing national practice guidelines. Implementing multidisciplinary guidelines for anxiety disorders was pursued against the background of a scientific study that as well as investigating the feasibility of implementing the guidelines, also aimed to assess the effectiveness of working according to the guidelines by using a prospective cohort design. At the start of this study, guideline adherence was too low to be able to make any meaningful comparison between the treatment results of patients that received guideline adherent care and those who did not. Successful implementation was thus a necessary step in performing this cohort study.

The treatment coordinator of the anxiety disorder unit was closely involved with this study and a key figure during the process of implementation. During the course of the study, a PhD student supervised by the treatment coordinator had an average of 16 hours per week available for facilitating the process of guideline implementation and the collection of data.

2.2.2. Dutch multidisciplinary guidelines for anxiety disorders

The multidisciplinary guidelines for anxiety disorders were first published by the workgroup for anxiety disorders in 2003. Based on a systematic evaluation of the scientific literature, the guidelines provide an overview of the state-of-the-art of care for patients with anxiety disorders, including hypochondriasis, ultimately reflecting the consensus of the expert group. As such, the guidelines for clinical practice are described for adult patients with a DSM-IV diagnosis of panic disorder with/without agoraphobia, social phobia, obsessive compulsive disorder (OCD), generalized anxiety disorder (GAD), posttraumatic stress disorder (PTSD), specific phobia and hypochondriasis.

Overall, the main evidence-based treatment steps recommended for the various anxiety disorders can be summarized as follows. According to the Dutch treatment guidelines for anxiety disorders both psychotherapy and pharmacotherapy count as equally valid treatment options. Recommended psychotherapeutic treatment steps consist of cognitive interventions or specific forms of exposure interventions. In cases of posttraumatic stress disorder, eye

movement desensitization reprocessing (EMDR) is also considered a valid first-choice treatment option. The first two or three treatment steps in pharmacotherapy consist of prescribing antidepressant medication. The guideline favors selective serotonin reuptake inhibitors (SSRIs) over tricyclic antidepressants (TCAs). In most cases, if an SSRI produces an insufficient result, switching to a second SSRI is recommended before prescribing a TCA. In cases of social anxiety disorder the third pharmacological treatment step is the prescription of a benzodiazepine or monoamine oxidase inhibitor (MAOI). In cases of obsessive-compulsive disorder that are resistant to treatment, the third step consists of augmentation of SSRI therapy with an atypical antipsychotic.

2.2.3. Measuring guideline adherence with the use of process indicators

One of the activities in the first phase of our project was the development of a set of process indicators as one of the two practical tools that help to provide input for the diagnostic steps in the implementation model. These indicators were developed [14] to gain an understanding of the degree of guideline adherence before the start of implementation and to monitor changes during the process of implementing the anxiety disorder guidelines. These process indicators reflect the percentage of patients receiving recommended care according to a specific guideline recommendation. However, the various anxiety disorder guidelines published in 2003 contained over 134 recommendations for clinical practice. The goal was to arrive at a workable number of indicators, based on the recommendations most relevant to improving the quality of care. An iterative consensus procedure was followed for this. The first step in developing the set of indicators was to select those recommendations that were based on the highest level of scientific evidence. This meant that only recommendations supported by the results of a systematic review, or by the results of at least two independently performed randomized clinical trials with sufficient sample size, were selected. Excluding four recommendations that related to the timing of a specific intervention, the number of selected recommendations was reduced to 38. These 38 recommendations were then reformulated into a preliminary set of indicators.

For instance, for patients suffering from a panic disorder with agoraphobia, the following recommendation: 'Exposure in vivo is an extremely effective intervention in the treatment of a panic disorder with agoraphobia. In those cases where avoidance plays an important part in the clinical picture of the disorder, there is no reason to apply a different psychological intervention than exposure in vivo a priori'; was reformulated into the process indicator: 'The

percentage of patients with panic disorder with (moderate) severe agoraphobia, indicated for treatment with exposure in vivo, that is offered exposure in vivo'.

In the next step a group of 18 expert clinicians, all members of institutions participating in the Dutch Knowledge Centre for Anxiety and Depression, were asked to judge this preliminary set of process indicators. The definite set of process indicators contained only the preliminary indicators that were judged relevant to clinical practice by 80% of those expert clinicians, and of which at least 60% said that the aspect of care covered by the indicator needed improvement in clinical practice. In this way, a set of 34 process indicators was obtained. These 34 indicators related almost exclusively to pharmacotherapy or cognitive-behavioural treatment of anxiety disorders. It was these forms of treatment that (besides EMDR for patients suffering from PTSD) survived the selection procedures, based on the level of scientific evidence and relevance to improving the quality of care as assessed by the expert group. This selection of indicators coincides with the first two or three steps of the psychotherapeutic and pharmacotherapeutic branches of the treatment algorithms for the various anxiety disorders. Thus the final selection of process indicators helps to measure whether the first two or three recommended treatment steps have been followed in each condition, if indicated.

For this study, the adequacy of psychotherapeutic treatment steps was assessed not only by looking at the percentage of patients receiving the right sort of treatment method. Three additional parameters were brought into the picture by using three supplementary help indicators, to measure the proper execution of each of these treatment steps. If the recommended psychotherapeutic treatment had been offered, these supplementary help indicators reflected: 1) whether a treatment rationale had also been given; 2) whether the accompanying homework assignments had been provided during at least half the sessions, where relevant, and; 3) whether the minimum recommended number of treatment sessions had been provided. The adequacy of the pharmacological treatment was not only assessed by looking at the prescription of the right category of medication. Here, three types of supplementary help indicators were also used. If the recommended type of medicine was prescribed, these reflected: 1) whether one of the specific drugs mentioned in the guideline had also been chosen (e.g. fluoxetine as one of the recommended SSRIs for patients with panic disorder); 2) whether the recommended dosage was prescribed and; 3) whether the drug was maintained long enough to be able to evaluate effective-

ness (to view an English translation of the final set of process indicators, and the corresponding supplementary help indicators see Appendice 1).

2.2.4. The development of a questionnaire to identify factors that could promote or impede guideline adherence

To gain an understanding of factors that could impede or promote the implementation of the guidelines from the professional's viewpoint, we developed a questionnaire [15] inspired by the theory of planned behaviour (TPB) [16]. We found inspiration in the example of Rebergen and colleagues [17], who developed a TPB-based questionnaire to examine predictors of adherence to guidelines for occupational physicians treating employees with mental health problems. The aim was to develop yet another tool, alongside the set of process indicators, that could be used in the diagnostic phase of implementing the multidisciplinary guidelines for anxiety disorders in other settings too.

To simplify, the TPB states that: 1) if people's attitude towards the suggested behaviour is more positive; 2) if they think that significant others want them to adopt the behaviour (subjective norm); 3) if they believe they are able to adopt the behaviour this results in; 4) then they will have a stronger intention (motivation) to adopt that behaviour, which makes it more likely that they will actually behave in that way. According to our application of the TPB, the target behaviour is adherence to the Dutch practice guidelines for anxiety disorders by the health care professional. We expected that knowledge of the position of the team members regarding each of the four TPB factors would be helpful when choosing concrete interventions to implement these anxiety disorder guidelines. Several items were formulated to measure each of these TPB constructs. To determine item topics relevant for the use with the anxiety disorder guidelines, 7 health care professionals from the anxiety disorder team were interviewed about factors that from their point of view could impede or promote the actual usage of the guidelines. Topics matching the TPB constructs were then reformulated into 58 items. Most of these took the form of concrete propositions, where the respondent was asked to rate his or her level of agreement on a five-point Likert scale (ranging from "I strongly disagree" to "I strongly agree"). Four of these 58 items asked whether the respondent actually possessed a copy of the multidisciplinary guidelines of anxiety disorders or a summary of it; whether the respondent had read the guidelines; and how the respondent rated his or her knowledge of the content of the guidelines. The answer to these questions were needed to assess how much effort should be put into disseminating the multidisciplinary guidelines for anxiety disorders.

To arrive at a more compact version of the questionnaire and establish the reliability of the different subscales, the original 58-item version of the questionnaire was distributed among 89 health care professionals that worked for one of the institutions participating in the Dutch Knowledge Centre for Anxiety and Depression. In analysing the data it was established that we succeeded in developing a reliable scale to measure the intention of the health care professionals to use the guidelines. After removing two items to further improve the reliability of the scale, we derived an 'intention' subscale consisting of five items. Subsequently, for the other three TBP based subscales, the five items that showed the best correlation with this intention scale were selected to form the definite scale of the corresponding construct. As such, three additional subscales were formed as follows: 1) 'Perceived behavioural control'; a scale that reflects the degree to which the health care professional expects to be able to arrange his or her work so that he or she can adhere to the recommendations in the guidelines. 2) 'Attitude'; a scale that reflects whether someone holds a positive or negative view of using the guidelines. 3) 'Social pressure'; a subscale that reflects the perceived social normative pressure to adhere to the guidelines. By doing this, together with the four questions about the possession, and knowledge of the guidelines and one question about how often the professional thought that he or she already used the guidelines, we derived a final 25-item version of the questionnaire to assess factors that could influence use of the guidelines by the professional. This 25-item version was considered to be short enough to be used easily in different treatment settings (to view an English translation of this version of the TPB questionnaire, see Appendice 2). Ultimately, it was this 25-item version of the questionnaire that was used within the anxiety disorder team of the community mental health centre of Almelo as part of the second diagnostic step of the implementation model see reference [15] for more details on the development of the questionnaire.

2.3. The process of implementing the guidelines

Following the steps suggested by Grol and Wensing , an implementation programme was designed specifically tailored to the situation in Almelo [13, 18]. The subheadings described below summarize the subsequent steps taken. For each subheading a description is given on how the corresponding step was developed for the anxiety disorder team.

Step 1: Analysing current practices and determining goals for improvement

We analysed the provision of care within the anxiety disorder team before starting to implement the guidelines by reviewing the medical records of 150 patients suffering from an anxiety disorder or hypochondriasis, who were treated between 2002 and the beginning of 2004. Checklists were used to assess the adherence to the relevant guidelines. The data collected in this way was used to score the set of process indicators described previously.

After reviewing the medical records of these 150 patients and scoring the appropriate indicators, the analysis showed that improvement was most needed on the adequate provision of cognitive interventions and exposure treatment. Relatively large numbers of patients received a positive indication for being offered this kind of treatment. However, only 15 per cent of patients in the case of cognitive interventions and only 17 per cent of patients in the case of exposure interventions did actually receive these kinds of treatment as they should have. A large number of patients that were being offered these kinds of interventions did not receive the corresponding homework assignments and did not undergo enough treatment sessions. So these aspects of care needed improvement. Also, improvement was necessary in the provision of EMDR for patients with PTSD. Compared to the provision of adequate psychotherapeutic treatment as first line of treatment, there was more adequate provision of the first step of pharmacological treatment. The most significant improvement in pharmacological treatment was deemed necessary in the more advanced steps of the medication algorithms, which however concerned only a small number of patients. Improving the number of patients receiving a recommended form of psychotherapeutic treatment was therefore considered to be the primary aim of implementing the guidelines.

Step 2: Analysing the context and target group for implementation

After analysing the actual provision of care and setting goals for improvement, we identified factors that could impede or promote guideline adherence at the level of the organization, the level of the health care providers and the level of the patients. A selection of seven team members with different professional backgrounds, were interviewed in depth about their opinion towards the anxiety disorder guidelines and factors that they thought may possibly impede their adoption. In addition, as part of the second step all of the team members were also asked to fill in the final 25-item version of this TPB questionnaire. The purpose of this was to assess the intentions of health care providers in using the

guidelines and to get a rough idea of the position of the team on each of the other three TPB constructs.

During the interviews, concerns were raised about two points. First the quality of the unit responsible for diagnosing newly referred patients and devising their treatment plans. The members of the anxiety disorder team had to adhere to this treatment plan to which patients had consented. Therefore it was deemed crucial that these treatment plans had to reach a higher standard and were to be modelled more according to the guideline recommendations. Second the interviewees also had the impression that they treated many patients with complex problems. They thought that the guideline recommendations would be difficult to apply to these patients and that this would impede guideline adherence.

Based on the data gathered using the TPB questionnaire, we were able to conclude that the team members held rather positive attitudes toward the guidelines in general. On the other hand they did not appear to feel much social pressure to follow guideline recommendations. Some of the team members also reported being unfamiliar with the exact content of the guidelines and many of the team members did not feel overly confident about being able to apply the guideline recommendations in daily clinical practice.

Step 3: The selection and development of implementation strategies

In step 2 we identified factors and circumstances that could impede or promote guideline adherence. These factors were found at different levels: organizational (the process of care and foremost the intake, diagnosing and choice of the treatment), patients (the matter of informed consent) and professionals (attitude towards the guidelines, the (felt) autonomy and the limited social pressure). Working on the different facets is one of the main characteristics of the overall approach and so we had to direct interventions on each of these facets.

At the organizational level it was obvious to us that some changes had to be made in how the intake procedure was organized. To improve the reliability of the diagnostic process, the idea was to make it compulsory to use the MINI, a semi-structured interview to derive at a DSM-IV diagnosis [19, 20], during the intake phase. It was also thought that it would be better if the treatment coordinator of the anxiety disorder team was made responsible for devising treatment plans for patients with an anxiety disorder or hypochondriasis. Consequently, the decision was taken that as soon as the member of the intake team had established an anxiety disorder or hypochondriasis as the primary

diagnosis, the patient would be referred to the anxiety disorder unit and scheduled for a meeting with the treatment coordinator to discuss the various treatment options. Doing this was expected to have two important advantages: 1) It would provide the best guarantee that the treatment plan would match the recommendations of the corresponding practice guideline, because the treatment coordinator would be involved in the process of implementing the guidelines; 2) The treatment coordinator would have an impression of all the patients treated within the unit, which could have added value when evaluating the course of treatment for individual patients during the bilateral treatment evaluations which were scheduled regularly. The expectation was that the treatment coordinator would be better able to help identify possible solutions for the problems mentioned by the therapist with applying the guideline recommendations, if he himself had also met the patient. This should lead to better guideline adherence.

At the patients level the intention was also to develop special patient instruction materials to educate the patient about their disorder and the various treatment options recommended in the corresponding practice guideline. This information was to be sent to patients prior to their meeting with the treatment coordinator. It was expected that it would be more difficult for the team members to ignore or overlook the course of action set out in the treatment plan if they knew that the method of treatment recorded in the plan reflected a considered patient choice.

At the level of professionals several interventions were planned to inform, instruct and commit. Two team meetings were organized to discuss the content of the guidelines. Educational materials for health care professionals, such as desktop versions of the guidelines summarizing the most important points of every guideline and the different treatment algorithms were developed. The purpose of this would be to improve the knowledge of the guideline recommendations considered most important for improving the quality of care on the part of the team members involved. We also intended to develop a treatment folder consisting of the psychological evidence-based treatment manuals that would be used the most frequently by the psychologists in the team, so that they would become accessible to all. Here the expectation was that this would make it easier for the psychologist to apply the recommended treatment methods. Several psychologists would also be sent for training in the use of EMDR because too few of the psychologists on the team were skilled in the use of this intervention. Finally, from the start of implementation, the health care professionals would also be asked to use a checklist with guideline recommendations

as the basis for the evaluation of the treatment progress of individual patients in the care of the team. This was to help keep the recommended treatment steps clearly in mind when deciding on a subsequent course of action.

Step 4: Executing the implementation plan

The health care professionals in the intake team were trained in using the MINI [19, 20]. The process of care was reorganized as suggested in step 3. Two team meetings were held to familiarize the health care providers with the content of the guideline. The first meeting was opened by the manager of the community mental health care centre to stress the importance of the implementation project. The development of the guidelines and its recommendations were both discussed at the meeting. It was emphasized that the guidelines had received the approval of the various professional bodies and the patient organization for people with anxiety disorders. Feedback was also given regarding the current provision of care within the anxiety disorder team by presenting the data derived from the medical records, and the goal for the future was explained: increasing the number of patients who receive a recommended form of psychotherapeutic treatment. It was explained that retaining positive scores on the defined supplementary help indicators was important to obtain a positive score on the main process indicator, by providing the corresponding homework assignments and sufficient number of treatment sessions in case of psychotherapeutic treatment. For pharmacological treatment, the importance of a positive score on the parameters covered by the pharmacotherapeutic help indicators was also emphasized.

Before the second meeting, the health care providers were asked to bring examples of patients from their caseload for whom they thought the guidelines would be difficult to apply. The purpose was to reach a consensus about the practical scope of the guideline recommendations and to reach a consensus about what would constitute legitimate reasons for deviating from the recommendations in the guidelines. By discussing the applicability of the guideline recommendations in these 'complex' cases, the opinion that the guideline recommendations could not be applied to most of the patients seen by the anxiety disorder team members also became less credible. The aforementioned instruction materials for patients and the different educational materials for the health care professionals in the anxiety disorder team were developed, tested and distributed according to plan. After the first team meeting, an evaluation of the treatment progress of individual patients in the regular team meetings on patient progress was carried out with guideline recommendations

clearly in mind. From that moment onwards, during each treatment evaluation the health care provider explained the course of treatment for the patient along the lines of the algorithms and the treatment coordinator would check guideline adherence. This was an aspect of quality assurance for the provision of optimal care. Also, several psychologists were invited to participate in a course about the use of EMDR with patients suffering from PTSD, as specified in the plan.

Step 5: Evaluating progress, and adjusting the original implementation plan

The last step of Grol and Wensing's model [13] consists of continuously monitoring the progress made. Six months after the start of the implementation, a third meeting was held to share experiences using the guidelines, get an impression of the team members' opinions about the course of the implementation project, and give feedback on the progress made in implementing the guidelines. At the time of this third meeting, most team members still had a positive attitude towards working according to the guidelines. However, some openly complained about having less autonomy and being less satisfied with their job since the start of the project. The impression was given that this was merely due to the increased supervision of their performance. Literature on this subject also shows a significant association between job autonomy and job satisfaction among health care professionals [21]. These signals were taken seriously. The treatment coordinator changed his style of asking about guideline adherence during treatment evaluations within the team, and the good intentions of the team members wanting to follow the guideline recommendations were taken more seriously. They were asked to talk about treatment progress and indicate themselves whether there were any difficulties in applying the guideline recommendations, without the treatment coordinator asking about guideline adherence proactively and most team members were satisfied with this arrangement. The first signals of an increase in the number of patients receiving the recommended psychotherapeutic care became apparent.

After one year, a sample of medical files was taken from fifty patients who had begun treatment after the implementation of the guidelines to evaluate the progress of implementation in greater detail. The data collected showed that the application of specific cognitive-behavioural techniques still seemed to pose a problem for some team members, although an overall increase in guideline adherence could already be discerned. Two additional team meetings were held. One focused on the use of behavioural experiments in cognitive therapy, in which automatic thoughts had already been tested several times with the use

of thought records and Socratic dialogue. This resulted in a first shift in the credibility of the anxious thoughts. The other meeting focused on new insight into the mechanisms of exposure treatment. In this meeting, the way this new insight could be translated into concrete homework assignments for patients with the various anxiety disorders was discussed from the start of therapy. The importance of motivating the patient to complete such assignments was emphasized.

Two years after the official start of implementing the guidelines, another review of medical files was carried out for 181 patients referred to the anxiety disorder team after October 2005 for a final evaluation of the implementation efforts. To assess changes in guideline adherence, a cross-section of the medical files from this second group of patients was taken midway through 2008. The original process indicators were scored once again. To increase power, aggregated information from the disorder-specific indicators was used where possible to reflect general changes in adherence to the recommended treatment steps. Table 1 reflects the patient characteristics of those patients included in the reviews of medical files before and after start of the implementation of the guidelines. As Table 2 shows, there is a significant difference in the number of asylum

Table 1. Socio-demographic and clinical characteristics of patients in the pre- and post-implementation group

	Pre-implementation group (n=150)		Post-implementation group (n=181)		p
Age: mean (SD)	34.0	(11.0)	33.9	(11.0)	0.94
Gender (female): n (%)	93	(62.0)	111	(61.3)	0.90
Living alone: n (%)	32	(21.5)	25	(15.7)	0.19
Educational level; elementary school, at max: n (%)	29	(19.3)	22	(13.9)	0.20
Foreign origin: n (%)	44	(29.3)	40	(22.1)	0.13
Asylum seeker: n (%)	24	(16.0)	12	(6.6)	< 0.01
Panic disorder: n (%)	58	(38.7)	71	(39.2)	0.92
Social anxiety disorder: n (%)	25	(16.7)	29	(16.0)	0.87
Obsessive-Compulsive disorder: n (%)	23	(15.3)	14	(7.7)	0.03
Generalized Anxiety disorder: n (%)	11	(7.3)	17	(9.4)	0.50
PTSD: n (%)	30	(20.0)	39	(21.5)	0.73
Specific phobia: n (%)	3	(2.0)	6	(3.3)	0.52
Hypochondriasis: n (%)	0	(0.0)	5	(2.8)	0.07

seekers treated within the anxiety disorder unit before and after implementation of the guidelines, probably due to the closure of a nearby refugee centre during that period. Also, fewer patients with OCD were seen for treatment after the start of implementation. Neither of these two variables were shown to be significantly associated with differences in guideline adherence however.

Table 2 shows the percentage of patients receiving treatment according to the recommended general treatment steps, before and after implementation of the guidelines and the change in percentage over time.

As can be seen in column 4 of Table 2, there were significant changes in the percentage of patients receiving cognitive interventions (+54.4%, $p < 0.01$) and the percentage of patients receiving the recommended form of exposure interventions (+42.7%, $p < 0.01$). Additionally, the percentage of patients with

Table 2. Guideline adherence in the pre- and post-implementation group

Guideline recommendation	Pre-implementation group (n=150)		Post-implementation group (n=181)		Difference (%)	p
Number of patients indicated for cognitive interventions and the percentage that actually received it: n (%)	124	(15.3)	109	(69.7)	+54.4	<0.01
Number of patients indicated for exposure interventions and the percentage that actually received it: n (%)	81	(17.3)	50	(60.0)	+42.7	<0.01
Number of patients indicated for treatment with EMDR and the percentage that actually received it: n (%)	23	(43.5)	30	(96.7)	+43.2	<0.01
Number of patients indicated for medication step 1 and the percentage that actually received it: n (%)	54	(55.6)	59	(61.0)	+5.4	0.56
Number of patients indicated for medication step 2 and the percentage that actually received it: n (%)	15	(20.0)	20	(45.0)	+25.0	0.12
Number of patients indicated for medication step 3 and the percentage that actually received it: n (%)	11	(45.5)	12	(16.7)	−28.8	0.19

posttraumatic stress disorder who were treated with EMDR, if indicated, was significantly higher (+43.2%, $p < 0.01$). Even though there were changes in the percentage of the patients being given adequate pharmacological treatment, the number of cases indicated for the different consecutive steps was too small to justify further statistical analyses.

2.4. Discussion and Evaluation

After drawing up a tailor-made implementation plan and using multifaceted implementation strategies, significant improvements in adherence rates to the Dutch multidisciplinary guidelines for anxiety disorders were found to have occurred. An increase was found in the number of patients being provided the recommended forms of psychotherapeutic treatment, which was the primary aim of the implementation activities. The delivery of adequate pharmacological treatment was not explicitly targeted for change and remained fairly stable. Generally, it seems that we may safely conclude that the implementation of evidence-based practice guidelines for anxiety disorders within mental health care is feasible.

Based on the experiences in our study, the implementation model of Grol and Wensing offers a useful approach to guideline implementation. It helps to plan and execute implementation activities systematically, and helps to develop implementation interventions that match the requirements of the target group. In our study, the factors that improved guideline adherence were interventions aimed at reorganizing the process of care, greater dissemination of knowledge about the guidelines (including the distribution of training materials to aid in following the guideline recommendations), and measures aimed at increasing normative social pressure in favour of adherence to the anxiety disorder guidelines.

The method of implementation described in this study appears to be effective, and can be easily copied by others. The preparation of implementation aids such as desk-top guides and the patient information materials is an idea that could easily be 'borrowed' from this study for use elsewhere. The same is true of the format of the team meetings and the training materials used. The questionnaire used to assess the health care providers' intention of beginning to use the guidelines can also be lend. Instead of the large sample needed for scientific research purposes, in daily practice small samples of about ten medical records can be used as input for the plan-do-check-act cycle to monitor progress in implementing the guidelines.

One limitation of the study is the use of before-and-after design to evaluate the effect of our implementation activities. Without the use of a control group and proper randomization procedures, we cannot conclude definitively that the changes in behaviour that we observed resulted from the efforts aimed at implementing the guideline. They may well simply reflect the passing of time and the fact that the use of guidelines became slowly more established in the Netherlands. Studies by Bauer [10] and Weinmann et al. [11] show, however, that without active efforts to ensure the implementation of a guideline, they will only be marginally adhered to. This casts doubt on the idea that the changes achieved merely reflect a process that would have happened anyway. Nevertheless, a controlled design is necessary to draw more firm conclusions about the effectiveness of the implementation activities such as those described here. Besides the evidence of the feasibility of implementing evidence-based guidelines for anxiety disorders, our results only allow the conclusion that the tailor-made approach presented here seems promising from the point of view of implementing evidence-based practice guidelines within mental health care.

A significant challenge however will be the maintenance of performance rates in the longer term. Health care professionals leaving the team and new personnel starting, and constantly changing organizational priorities will make this a difficult task. The treatment coordinator – a key figure in ensuring proper guideline adherence – left at the end of the study. The impression was that adherence rates dropped slightly after this. It is very important to continue monitoring guideline adherence and provide continuous feedback. With new personnel coming in, it is necessary to hold regular training days such as those held at the start of the implementation. Our impression is that doing so would prove very worthwhile. The multifaceted approach also seems to be specifically relevant in meeting this challenge because of the different factors which intervene and interact: organizational (for instance organizational rules and leadership), professionals (information, education, instruction and commitment) and the patients level (information, participation). Measures have to be taken at the different facets to maintain the necessary change.

2.5. Conclusions

The case study presented here shows that the implementation of practice guidelines for anxiety disorders in mental health care is feasible. After drawing up a tailor-made plan for implementation and using multi-faceted implemen-

tation strategies, significant differences were found on those aspects of care that were targeted for change in the community mental health care centre in which this type of guidelines were implemented. The study also shows, however, that it is important to think about ways to maintain changes made in the provision of care in the longer term. An important question remains whether following such anxiety disorder guidelines does indeed lead to better treatment outcomes, as expected. A future publication will report on the relationship between adherence to such guidelines and treatment outcomes, based on the treatment results gained in patients treated in the community mental health care centre after the start of the activities aimed at implementing the guidelines.

Abbreviations

TPB, Theory of planned behaviour; OCD, Obsessive compulsive disorder; GAD, Generalized anxiety disorder; PTSD, Posttraumatic stress disorder; SSRI, Selective-Serotonin-Reuptake-Inhibitor; TCA, Tri-Cyclic-Antidepressant; SNRI, Serotonin-Norephinephrine-Reuptake-Inhibitor; MAOI, Mono-Amine-Oxidase-Inhibitor

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CHAPTER 3

The effectiveness of adhering to clinical-practice guidelines for anxiety disorders in secondary mental health care: the results of a cohort study in the Netherlands

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Abstract

Background: While studies into the implementation of clinical practice guidelines for mental health care are scarce, studies on the effectiveness of implementing practice guidelines for anxiety disorders appear to be entirely nonexistent.

Objective: To examine whether adherence to anxiety disorder clinical practice guidelines in secondary mental health care yields superior treatment results than non-adherence.

Method: A closed-cohort study of 181 outpatients with an anxiety disorder or hypochondriasis who were treated in a routine mental health setting. Preceding the inclusion of these 181 patients, a start was made on the implementation of the Dutch national multidisciplinary practice guidelines for anxiety disorders. Patients were asked to complete several questionnaires before the start of treatment and again one year later. The medical records of these patients were reviewed to assess guideline adherence. Ultimately, adherence or non-adherence to the different treatment algorithms described in the guidelines was related to changes in the severity of psychiatric symptomatology, psychiatric functioning, general well-being and satisfaction with treatment.

Results: Compared with patients whose treatment did not adhere to the guidelines, those whose treatment adhered to the guidelines were found to have greater symptom reduction after one year ($p<0.01$). The latter group of patients also rated their satisfaction with their treatment significantly higher ($p=0.01$). No significant differences were found after one year with respect to changes in impairment of functioning and quality of life in the two groups of patients.

Conclusions: Adherence to anxiety disorder guidelines yields superior treatment results and increased patient satisfaction with treatment when compared with patients whose treatment did not adhere to the clinical guidelines. These results should encourage a more widespread implementation of such guidelines in mental health care facilities.

Keywords

Anxiety disorders, guidelines, effectiveness

3.1. Introduction

In order to reduce unwanted variance in the provision of care and to promote the use of empirically supported treatment methods, clinical practice guidelines for mental health care have been developed in many countries over the last decade. The use of these guidelines is expected to improve the quality of care by promoting evidence-based practice. However, few studies have been conducted into the implementation of such guidelines. Two reviews on the effect of implementing guidelines on provider performance and patient outcomes within mental health care found that various implementation strategies are moderately effective, at best [1, 2]. The best results seem to be produced by implementation studies that use complex multi-faceted interventions and have been developed specifically to overcome certain barriers to change in the context of the particular implementation study. However, many studies conclude that the positive results on provider behaviour are only temporary [1, 2]. These results show that implementing treatment guidelines within psychiatry often proves difficult, despite the potential for improvements to the quality of care.

The Netherlands was among the first countries to develop practice guidelines for mental health care, with more than ten different multidisciplinary guidelines published since 2003 [3]. The first guidelines that were published, under the auspices of the Dutch national steering committee for multidisciplinary guideline development in mental health care, concerned the treatment of anxiety disorders and hypochondriasis [4]. Despite the availability of effective psychotherapeutic and pharmacological treatments, a large proportion of patients with anxiety disorders still do not receive an evidence-based form of treatment in the Netherlands [5-7], as is true in many countries. Implementing evidence-based clinical practice guidelines should change that.

While studies on implementing clinical practice guidelines in mental health care are scarce, studies on the effectiveness of implementing practice guidelines for anxiety disorders appear to be nonexistent. Recently, we performed a study that showed that it is feasible to implement such guidelines [8]. After drawing up a tailor-made implementation plan and using multifaceted implementation strategies, significant improvements in adherence rates to the Dutch multidisciplinary guidelines for anxiety disorders were found in the community mental health care centre in which these guidelines were implemented [8]. However, the question of whether implementing such anxiety disorder guidelines yields better treatment results remained unanswered. We hypothesized

that the use of treatment guidelines should improve treatment outcomes. As part of the evaluation of the implementation of the anxiety disorder guidelines within the fore mentioned health care centre, we investigated whether there was any relationship between guideline adherence and treatment response one year after the start of the treatment. This when the data about the treatment results gained became available.

3.2. Methods

3.2.1. Study design

A cohort was formed of patients who were registered at the community mental health care centre in Almelo (a town in the east of the Netherlands) after start of the implementation of the Dutch multidisciplinary practice guidelines for anxiety disorders within this centre. Activities aimed at implementing the guidelines began in October 2005. From that moment, 181 newly registered patients with an anxiety disorder or hypochondriasis were included. The last patient was included in July 2007. Of this group of 181 patients, those who were sufficiently fluent in Dutch were asked to fill in several questionnaires before beginning treatment and again one year later. The medical records of these patients were reviewed to assess adherence to the treatment guidelines. In this cohort, adherence to the treatment guidelines correlated with a reduction in the severity of the patient's psychiatric symptomatology, decreases in the impairment of social functioning, improvements in general well-being and satisfaction with treatment.

3.2.2. Research setting

The community mental health centre where the Dutch multidisciplinary practice guidelines for anxiety disorders were implemented is located in the town of Almelo in the east of the Netherlands. The treatment centre is part of a larger organization, including (semi-)clinical settings, which is the main provider of mental health care in the region. The community mental health care centre provides ambulatory care and is structured into several disorder-specific units. After being referred to the centre by their general physician, patients undergo a general intake procedure. On the basis of the primary diagnosis, the patient is allocated to a disorder-specific unit where treatment takes place. The unit responsible for the treatment of anxiety disorders has 16 team members, including a psychiatrist and several psychologists and psychiatric nurses. The

experience of the team members in providing health care ranged from beginner's level to very experienced. The mean age of the team members was 35 years (range 24-53 years).

In implementing the anxiety disorders guidelines the steps as suggested by Grol and Wensing were followed [8, 9]. The preparations for implementing the guidelines began at the end of 2004, almost a year before the official kick-off for the start of the implementation of the guideline and the inclusion of patients that formed the cohort in which the effectiveness of using the guidelines was investigated. Ultimately, based on a diagnostic analyses of possible barriers for implementation in the target setting a tailored made plan for implementation was designed that comprised the following main interventions: 1) the reorganization of the care process in which the treatment coordinator –an experienced cognitive behaviour therapist- of the anxiety disorder team would see all patients allocated to the unit at the start of their treatment. So, the treatment coordinator was made responsible for devising the treatment plan for all patients allocated to the unit instead of the intake professional. This to ensure that the treatment plan would match the recommendations of the corresponding practice guideline. 2) The development and distribution of instruction materials for patients and health care providers 3) The organisation of two educational meetings in which the content of the guidelines were discussed. 4) The training in the skills needed to perform treatments suggested in the guidelines e.g. a selection of the psychologists were trained in the use of eye movement desensitization reprocessing (EMDR) for patients suffering from posttraumatic stress disorder [8].

During the time the patients were included in the study, activities aimed at implementing the guidelines were continued to further promote guideline adherence. The evaluation of treatment progress of individual patients in the regular team patient-progress meetings was done with help of a guideline recommendations checklist. Further, additional educational meetings were held in the team to improve the knowledge and use of specific cognitive behavioural techniques and corresponding homework assignments. As part of the cycle for continuous quality improvement for which at regular intervals data about guideline adherence was collected, it was found that these aspects of care needed extra attention in our treatment setting.

3.2.3. Patients

All consecutively referred patients between 18-65 years with a primary DSM-IV diagnosis of panic disorder with/without agoraphobia, social phobia, OCD,

generalized anxiety disorder, PTSD, specific phobia or hypochondriasis were eligible for inclusion in the study. In accordance with the guidelines, no further exclusion criteria were formulated. The Mini International Neuropsychiatric Interview (M.I.N.I.) [10, 11] was used to assess DSM-IV diagnoses. Patients were asked to provide informed consent in writing. The study was approved by the medical ethics committee of the VU University Medical Center.

3.2.4. The Dutch multidisciplinary guidelines for anxiety disorders

The Dutch anxiety disorder guidelines are based on evidence based principles. According to these guidelines, anxiety disorder patients may be treated with either psychotherapy or pharmacotherapy, both of which count as equally valid options [4]. Regardless of the specific anxiety disorder, recommended psychotherapeutic treatments consist of cognitive therapy or behaviour therapy (e.g. exposure in vivo). In post-traumatic stress disorder (PTSD), eye movement desensitization reprocessing (EMDR) is also considered to be a valid first-choice treatment option. Applied relaxation is recommended for patients suffering from panic disorder or generalized anxiety disorder that do not respond to cognitive-behavioural interventions. According to the Dutch anxiety disorder guidelines, the first three treatment steps in pharmacotherapy consist of prescribing three types of antidepressants. The guidelines favour selective serotonin reuptake inhibitors (SSRIs) over tricyclic antidepressants (TCAs). If an SSRI proves insufficient, switching to a second SSRI is recommended before prescribing a TCA. However, for a patient suffering from generalized anxiety disorder (GAD) the prescription of the SNRI venlafaxine is recommended instead of a second SSRI. In social phobia, the third pharmacological treatment step is the prescription of a benzodiazepine or monoamine oxidase inhibitor (MAOI) rather than a TCA. In treatment-resistant obsessive-compulsive disorder (OCD), the third step consists of augmenting SSRI therapy with an atypical antipsychotic.

3.2.5. Measuring guideline (non-)adherence

We used process indicators that reflected the percentage of patients receiving the recommended care according to a specific guideline recommendation. These indicators represented guideline recommendations based on scientific evidence of the highest quality and of the most relevance to improving the quality of care. The indicators were selected by consensus by senior professionals at the Dutch knowledge centre for anxiety and depressive disorders [8, 12]. The selected indicators coincide with the first two or three steps of

the psychotherapeutic and pharmacotherapeutic branches of the treatment algorithms for the various anxiety disorders. Effectively, then, the indicators measure whether the first two or three recommended psychotherapeutic and pharmacotherapeutic treatment steps have been followed adequately for each anxiety disorder.

During the review of the medical files, a specially developed checklist was used to determine the scores on relevant process indicators. This checklist was applied to the first 100 medical files by two assessors. Differences between the coding forms were resolved by reviewing the original files, leading to one coding form per medical file. In the case of uncertainty about how to score a certain process indicator, a consensus was reached through discussion with members of the study group (MKvD and DBO). Applying the same decision rules as with the first 100 files, an additional 81 medical files were reviewed by one of the assessors.

The adequacy of psychotherapeutic treatment steps was assessed not only by looking at whether the right sort of treatment was provided, but also other criteria such as the presence of a treatment rationale, accompanying homework assignments, and the recommended minimum number of treatment sessions. In assessing the adequacy of the cognitive-behavioural treatment provided for anxiety disorders, the use of this kind of minimal therapy criteria have also been used by others (see [13, 14]). The adequacy of the steps in the pharmacological treatment was assessed on whether the right category of medication had been prescribed and whether one of the specific drugs mentioned in the guidelines had been chosen. Then the dosage and maintenance of the medication were evaluated. If a positive score was obtained for each of the parameters mentioned above, an overall score for the relevant treatment step was given.

When assessing adherence to the treatment guidelines, an indicator was only scored if the guideline recommendation on which it was based was indicated for that specific patient at that particular time. The specific recommendation could also be judged to be inapplicable or even contraindicated. For instance, a specific recommendation was contraindicated in the following cases: when the primary diagnosis was revised; when a patient refused care; when another recommended form of treatment had just started; when a sufficient response to the treatment had already been achieved; or when psychosocial problems, suicidality or addiction problems had to take priority. In cases of pharmacological treatments, too, severe side effects or somatic contraindications were legitimate reasons for deviating from recommendations of the treatment guidelines. It was also possible that patients could drop out of therapy, render-

ing it impossible for the professional to provide adequate care. In all of these instances, the specific guideline recommendation was deemed inapplicable and the corresponding indicator was left without a score. Ultimately, adherence to the treatment algorithms described in the treatment guidelines was defined dichotomously (yes or no). If the algorithm was followed correctly and all the necessary steps in the treatment had been taken, the case would receive the label "adherent".

3.2.6. Outcome variables

The severity of psychiatric symptoms was measured using the Symptom Checklist (SCL-90-R) [15, 16]. Changes to the total score on the SCL-90-R from baseline to one year after the start of treatment constituted the primary measure of outcomes in this study. Three secondary outcome measures were also used: changes in the impairment of functioning were measured using the Sheehan Disability Scale (SDS) [17]; changes in reported quality of life were assessed with the use of the World Health Organization Quality Of Life questionnaire (WHOQOL- BREF) [18]; and finally, the Dutch national instrument for measuring patient satisfaction with mental health care was used one year after the start of treatment (GGZ Thermometer) [19].

3.2.7. Potential confounders and effect modifiers

Demographic variables such as age, gender, ancestry and educational level were considered as potential confounders or effect modifiers. Other co-variables that were considered were: 1) co-morbid depressive symptomatology, measured with the 30-item Inventory of Depressive Symptomatology (Self-Report) [20], and 2) the presence and severity of symptoms of a personality disorder, assessed with the use of the Personality Diagnostic Questionnaire (PDQ-4) [21, 22].

3.2.8. Statistical analysis

Standard descriptive statistics were used to describe the study population. At baseline, the group of patients who were not treated in adherence with the treatment guidelines were compared with t-tests for continuous variables and χ^2 tests for proportions with the group of patients who were treated in adherence with the guidelines on characteristics that could affect outcome. The influence of adherence on outcomes was assessed using regression analyses. Because change in the severity of symptoms expressed as a raw change score from baseline to one-year follow-up may not be reliable [23], a "residual gain

score" was calculated on the outcome variables [24, 25]. To do this, a simple regression analysis was performed first, with the test score at baseline as the independent variable and the test score at one-year follow-up as the dependent variable. This procedure was repeated for the three outcome measures. In each case, the residual gain score was used as the dependent variable in multiple regression analyses to determine the impact of guideline adherence, the central independent variable. To rule out possible bias through confounding, variables by which the treatment-adherent and treatment-non-adherent groups differed from one another were added to the regression analysis, in addition to the central independent variable. If adding one of these variables led to a 10% change in the regression coefficient of the central independent variable, this variable was designated as a relevant confounder that needed to be accounted for. All calculations in this study were performed with SPSS, version 15.0 (SPSS Inc., Chicago IL).

3.3. Results

Figure 1 shows the number of patients found to be eligible for inclusion in the study after the start of the implementation of the treatment guidelines in the community mental health care centre. A total of 181 patients gave informed consent for participation in the study. Twenty-one of these patients (11.6%) were not fluent in Dutch and were therefore unable to fill in the questionnaires. Of the remaining 160 patients, the treatment guidelines turned out to be inapplicable to 21 patients, because of an early revision of their diagnosis or because they dropped out of therapy. This left 139 patients (86.9%), in which one or more of the recommended treatment steps in the guidelines should be followed and to which the guideline recommendations were considered applicable. Of these 139 patients, 58 patients (41.7%) belonged to the guideline-non-adherent group, while 81 (58.3%) patients belonged to the guideline-adherent group.

Table 1 shows the characteristics of the guideline-adherent group and the guideline-non-adherent group in the sample of 139 patients. Patients in the non-adherent group lived alone significantly more often than patients in the guideline-adherent group. Age, gender, educational level or ethnic background did not differ significantly between the two groups. Adherence to the treatment guidelines was significantly lower in patients with more severe psychopathology, as reflected by higher scores on SCL-90-R, IDS and PDQ-4.

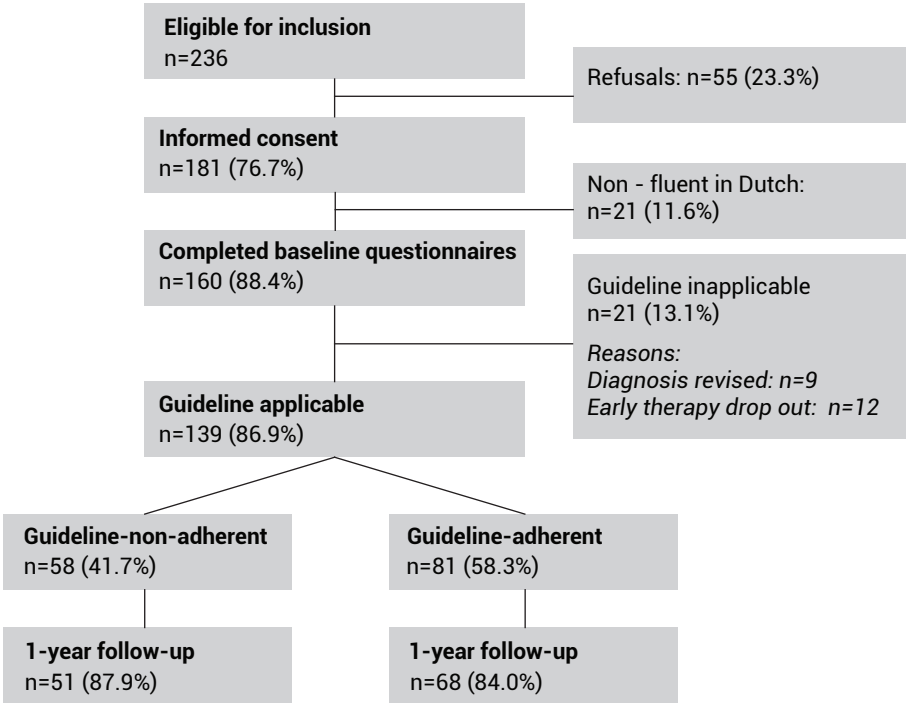

Figure 1. Flow chart for patient inclusion

It was also found that non-adherent treatments comprised significantly more treatment sessions compared to guideline-adherent treatments. Because of these differences between the adherent and non-adherent groups, we carried out a check on whether these variables were confouding the relationship between guideline adherence and treatment outcomes. Only the number of treatment sessions proved to be a relevant confounder for the different outcome measures of the study. On average, patients whose treatment did not adhere to the guidelines were seen more often in the period of sample. A negative correlation was found between the number of treatment sessions spent on a patient and treatment outcome.

3.3.1. Primary outcome measure

The multiple regression analysis examining the association between guideline adherence and changes in general psychopathology (i.e. the residual gain score for changes in SCL-90-R total score), after partialling out the effect of number of treatment sessions, produced a β= -32.14 (p=0.02). This indicates that the average treatment gain on the SCL-90-R total score was more than

Table 1. Characteristics of the patients in which the treatment guidelines were adhered to or not (n=139)

	Non-adherent (n=58)		Adherent (n=81)		p
Age: mean (SD)	33.86	(10.8)	33.51	(12.0)	0.86
Gender (female): n (%)	30	(51.7)	52	(64.2)	0.14
Living alone: n (%)	13	(22.8)	8	(9.9)	0.04
Educational level; only elementary school. or less: n (%)	7	(12.5)	11	(13.6)	0.85
Foreign origin: n (%)	9	(15.5)	8	(9.9)	0.32
Panic disorder: n (%)	22	(37.9)	31	(38.3)	0.97
Social anxiety disorder: n (%)	10	(17.2)	16	(19.8)	0.71
Obsessive-Compulsive disorder (OCD): n (%)	5	(8.6)	5	(8.6)	0.97
Generalized Anxiety disorder (GAD): n (%)	6	(10.3)	6	(7.4)	0.54
Post-Traumatic Stress Disorder (PTSD): n (%)	13	(22.4)	16	(19.8)	0.70
Specific phobia: n (%)	1	(1.7)	3	(3.7)	0.64
Hypochondria: n (%)	1	(1.7)	2	(2.5)	1.00
SCL-90 T0 score: mean (SD)	216.9	(77.4)	192.8	(60.8)	0.04
IDS score T0; severe depression yes: n (%)	20	(35.1)	14	(17.3)	0.02
PDQ-4 score; personality disorder probable: n (%)	29	(58.0)	29	(40.3)	0.05
Number of face to face contact with members of the anxiety disorder team: mean (SD)	25.9	(17.3)	17.4	(12.0)	<0.01

32 points greater among the group of patients whose treatment had adhered to the treatment guideline recommendations compared to the patients in the non-adherent group.

3.3.2. Secondary outcome measures

Adherence to the guidelines did not significantly influence the change in the global impairment of functioning, quality of life and general health. None of the multiple regression analyses reached significance. On all these variables a significant improvement was found (all $p < 0.01$); however, this improvement was not significantly related to guideline adherence.

At one-year follow-up, the patients in the adherent group were significantly more satisfied with their treatment than patients in the non-adherent group (7.73 versus 7.17; $t=2.545$, $df=115$, $p=0.01$).

3.4. Discussion

Patients who received guideline-adherent treatment showed significantly greater symptom reduction as measured with the SCL-90-R. It seems that omitting or withholding a recommended treatment step can be viewed as a missed opportunity to improve a patient's general psychopathology. On average, a significant improvement in functioning, patient-reported quality of life and general health was achieved across the total sample of patients. The influence of guideline-adherent care concerning these aspects was not significant, however. The fact that patients who received guideline-adherent treatment reported more satisfaction with their treatment can be seen as an incentive to follow the guidelines more often in routine practice.

The results of our study therefore show that guideline adherence does matter, not only with regard to alleviating symptoms, but also when it comes to treatment satisfaction and possibly also treatment efficiency too. In our sample, which is representative of routine secondary mental health care in the Netherlands, it was also established that the guidelines should be applicable to 87% of the patients seeking help. All these findings should encourage the more widespread implementation of the guidelines in mental health care facilities.

Some of the Dutch multidisciplinary guidelines for anxiety disorders that were investigated in this study have been recently revisited [26]. This has led to some minor adjustments mainly concerning the provision of so-called basic interventions, self-help methods and sometimes e-health as first line of treatment. These are usually provided in primary care for patients seeking help, and some of the more advanced steps in the medication algorithms. The implications of these adjustments for clinical practice within secondary care, as provided within the community mental health care centre, is limited. This study is therefore still deemed relevant for secondary care, although its focus is the implementation of the original anxiety disorder guidelines that were published in 2003.

Because this study found that adherence to the treatment guidelines was significantly lower among patients suffering from more severe psychopathology, one could conclude that guidelines can only be delivered in a sample of patients with less severe symptoms or without comorbidity. However, within the sample of patients whose treatment adhered fully to the guidelines, no differences were found between the subgroups with milder and more severe symptoms with respect to treatment results gained. This suggests that the use of the guidelines to treat more severe patients is not necessarily contraindicated.

In some cases, however, it is necessary to provide additional help or support in clinical practice in addition to the recommended treatment options. The help of a psychiatric nurse may be warranted to prevent problems relating to the social environment of the patient from becoming a problem. Offering admission to a crisis support service is also a prerequisite for patients who are suicidal. The provision of this type of additional support does not preclude adherence to the anxiety disorder guidelines. From the perspective of the health care provider, applying the recommendations in the guidelines to these patients does seem especially challenging, however. More knowledge of how this can best be achieved is still to be uncovered.

A limitation of the study is the uncontrolled design that we used. In cohort studies, the influence of confounding factors must be taken into account. We corrected for demographic variables and comorbidity of depression and symptoms of a personality disorder. However, in uncontrolled cohort studies, one should be cautious of making causal inferences about the effectiveness of the intervention, e.g. the provision of treatment according to the guidelines. To our knowledge, this is the first study that has looked at the added value of guidelines for anxiety disorders in clinical practice. The study results justify further investigation of the effectiveness of implementing anxiety disorder guidelines in a controlled design.

This study also used reports in the medical files as a proxy for guideline adherence. It is possible that these notes will only provide an indirect impression of the treatment actually delivered. However, this proxy measure of guideline adherence was chosen because it is less invasive than more direct measures in which audio or video recordings of treatment sessions are used to assess treatment integrity. Similar measures to those used in this study were also recently used by the Department of Veteran Affairs in the United States for a comprehensive evaluation of its mental illness and substance use treatment system [27] and the use of performance indicators based on data from the patient's medical records would seem to provide an acceptable way of making global judgements of the quality of care.

We assessed the quality of treatment using a number of clinically important variables, such as the provision of an accompanying treatment rationale, the provision of adequate homework assignments in half of the sessions and the provision of sufficient treatment sessions in cases where cognitive or behaviour therapy had been included in the patient's treatment plan. As mentioned earlier, this type of assessment has been used before to assess CBT. To ensure the reliability of the adherence scores, we used standardized checklists.

Future research into the effectiveness of guideline adherence should also investigate factors that influence treatment prognosis. A percentage of patients who received guideline-adherent treatment showed no significant symptom reduction; the symptoms of some patients even deteriorated. Knowledge about how prognostic factors influence outcome will help to make the provision of care more efficient, especially where it is known which recommended treatment steps would most benefit patients with certain symptoms, and which steps should be avoided. At a time of increasing health care expenditure and shrinking budgets, this is the type of research that is needed most.

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Chapter 4

Effectiveness of the implementation of treatment guidelines for anxiety disorders in specialized mental health care

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Abstract

Objective: To examine the effect of implementing anxiety disorders guidelines on guideline adherence and patient outcomes in specialised mental health care.
Method: A treatment setting in which guidelines were implemented (intervention condition) was compared to one in which guidelines were only disseminated (control condition).
Results: 61.7% of 81 intervention-condition patients received treatment according to the guidelines vs. 40.6% of 69 control-condition patients (p=.01). At 1-year follow-up, intervention-condition patients showed a greater decrease in anxiety symptoms (d=.48, p<.05); higher percentages of response (52.6% vs. 33.8%;p=.025) and remission (33.3% vs.16.9%;p=.026); and a greater decrease in the rate of phobic avoidance (d=.34, p<.05). At 2-year follow-up, control-condition patients had experienced a longer period of treatment, which had eroded most of these differences, except for phobic avoidance.
Conclusion: Systematic guideline implementation results in earlier gains and shorter treatment times.

Significant Outcomes

- Systematic implementation, in addition to passive dissemination of guidelines for anxiety disorders, seems to promote guideline adherence and improve treatment outcomes.
- Small to medium between group effect-sizes were found on measures of anxiety and avoidance behaviour at 1-year follow-up, when comparing the intervention and control condition.
- At 2-year follow-up, due to continuous treatment patients in the control condition seem to largely catch up in terms of the obtained treatment results. From a long-term perspective, anxiety disorder guideline implementation might improve efficiency of care.

Limitations

- Due to the observational nature of this study and the lack of a proper randomization procedure, this limits the possibility of making firm causal inferences.
- Although additional check-ups for the influence of bias by confounding yielded that the measured variables did not really threaten validity of the study results, both study conditions cannot be said to be completely similar with respect to the setting and patients treated there.
- The method of reviewing the patient's medical record to assess guideline adherence, can only provide an indirect estimate of the actual performance of the involved healthcare providers, and requires interpretation by the reviewer.

4.1. Introduction

Despite the existence of a large number of evidence-based treatment guidelines for mental health care, only a few studies have evaluated the effectiveness of implementing these guidelines. A recently performed systematic review concluded that the effectiveness of implementing psychiatric guidelines was not unequivocal [1]. This review included 18 comparative guideline implementation studies concerning a range of psychiatric diagnoses, and of diverse methodological quality. From this review it appeared that the effects on provider behaviour and patient outcome were at best modest and in most cases of limited duration [1]. Furthermore, the type of diagnosis seemed to critically influence the magnitude of treatment outcome obtained by successful implementation. According to the authors, in contrast to severe mental illness (SMI), such as schizophrenia and dementia, depressive disorders could be a more favourable area of mental health care for improving outcomes through the implementation of guidelines [1]. They suggested that the treatment of SMI is more complex than that of depressive disorders and improving treatment for SMI might therefore demand more effort. Indeed, three recent studies have confirmed the positive effects of implementing treatment guidelines for depressive disorders [2, 3, 4].

Since anxiety disorders have many clinical characteristics in common with depressive disorders, implementing treatment guidelines for these types of disorders might also be a successful way of improving outcomes. Anxiety disorders constitute a highly prevalent group of mental disorders and are known to compromise quality of life markedly [5]. A significant proportion of patients with anxiety disorders do not receive an evidence-based form of treatment [6, 7, 8]. A study by Andrews et al (2004) suggests that providing optimal care for anxiety disorders to all patients would improve the cost-effectiveness of healthcare [9]. This study however was based on a modelled scenario, so further research is necessary to support such a claim. It was only recently found to be feasible to actually implement treatment guidelines for this group of patients in specialised mental health care [10].

Because the effect of implementing anxiety disorders guidelines on outcomes at the patient level has not yet been empirically assessed, we compared the effects of implementation vs. dissemination of these guidelines in two settings. We hypothesized that the implementation of anxiety disorders guidelines in specialised mental health care would lead to higher degrees of guideline adherence and to superior outcomes.

Aims of the study

To examine the effect of implementing anxiety disorders guidelines on guideline adherence and patient outcomes in specialised mental health care

4.2. Method

4.2.1. Design

In this 2-year implementation study, we compared two types of strategies to promote guideline adherence in two specialised mental health care centres and studied (i) the adherence to the anxiety disorders guidelines by professionals and (ii) the effect on the presence and severity of anxiety and depressive symptoms in patients. Outcome measurements took place at baseline and at a 1-year and 2-year follow-up. The study was approved by the medical ethics committee of the VU University Medical Centre Amsterdam.

The anxiety disorder guidelines were implemented in a specialised mental health care centre in Almelo (intervention condition). Implementation was defined as 'a planned process and systematic introduction of innovations and/or changes of proven value, in the function of organizations; the aim being that these are given a structural place in professional practice, in the functioning of organizations or in health care structures' [11]. The control condition, in which the guidelines were only disseminated, took place in a specialised mental health care centre in Amsterdam. Dissemination was defined as 'the process of communicating information to care providers only, this to increase their knowledge and skills' [12]. The data from the control condition were derived from the Netherlands Study on Depression and Anxiety (NESDA), a naturalistic cohort study on the long-term course and consequences of depressive and anxiety disorders [13]. Data from the control and intervention conditions were gathered using the same procedure during the same period.

4.2.2. Comparability of the two treatment settings

Around the time of the start of the patient inclusion for the study from the beginning of 2005, the community of Almelo contained 72, 293, and the community of Amsterdam 742, 783 inhabitants. Of the population of 15 till 65 year-olds in Almelo, 36% had a lower educational level, 45% a middle educational level and 19% a higher educational level. In Amsterdam, 24% had a lower educational level, vs. 33% with a middle educational level, and 41% with a higher educational level (2% unknown). The average disposable income per

household was euro 26, 200 in Almelo vs. euro 26, 100 in Amsterdam (excluding students) (www.cbs.nl).

The two participating treatment centres of the study were both specialised in treating anxiety disorders. The centres were comparable in terms of the number (16 vs. 17 persons), age (mean 35 years (range 24-53) vs. 41 years (range 26–57)) and type (psychiatrists, psychologists and psychiatric nurses) of health care professional staff. In the intervention condition, the percentage of male professionals was 43.8% vs. 25.0% in the control condition. The professionals working in the two units included the complete range from novice to very experienced health care providers, although in the control condition the staff had slightly more seniority, especially the psychologists working there.

Using a specially developed questionnaire [10, 14], data on additional factors that may have a positive or negative effect on guideline adherence were collected from the health care professionals in both conditions before the start of implementation in the intervention condition. This questionnaire was inspired by the theory of planned behaviour (TPB) [15] and consisted of four subscales assessing (i) the attitude towards the guideline, (ii) the intention to use it, (iii) the perceived social pressure to adhere to the guideline and (iv) perceived control over work processes in order to be able to adhere to the guideline. These subscales represented the main TPB constructs, with possible scores ranging from 1 to 5 (with 5 signifying a higher score). In addition, the questionnaire also asked the professional to rate his or her knowledge of the content of the guidelines.

The results showed that the professionals in both conditions held an equally positive view of the use of guidelines ('attitude' subscale: intervention: Mean 4.1 (SD=.63) vs. control: Mean 4.3 (SD=.36); t=.71;df=20;p<.485) and expressed equally strong intentions to continue or start working according to the guidelines ('intention' subscale: intervention: Mean 4.0 (SD=.50) vs. control: Mean 4.1 (SD=.28); t=.46, df=22;p=.652). The professionals in the intervention condition judged their knowledge of the content of the guidelines to be significantly inferior to the professionals of the control condition (Mean 2.3 (SD=1.19) vs. Mean 3.4 (SD=.51); Mann-Whitney U=33.0; p=.017). They also perceived significantly lower social pressure to adhere to the guidelines (intervention: Mean: 3.4 (SD=.47) vs. control: Mean 3.9 (SD=.36); t=.2.83, df=21;p=.01). Finally, the professionals in the control condition expected to be better able to arrange their work so that they could easily adhere to the guideline recommendations ('perceived behavioural control' subscale: intervention: Mean 3.7 (SD=.54) vs. control: Mean 4.3 (SD=.29); t=.3.52, df=21;p<.01).

4.2.3. Eligibility criteria

As part of everyday care, after referral by their general practitioner, patients in both the intervention and control conditions underwent a standardized intake procedure. In this study we included outpatients aged 18 through 65 years who were (i) diagnosed with the Composite Interview Diagnostic Instrument (CIDI [16]) with one of the following DSM-IV anxiety disorders as primary diagnosis: panic disorder with or without agoraphobia, social phobia or generalised anxiety disorder (GAD) and who (ii) gave written informed consent for participation. Co-morbidity with other mental disorders was allowed. In patients with co-morbid mental disorders the primary diagnosis was defined as the psychiatric disorder with the most associated suffering for the patient. In order to maintain representativeness, only two exclusion criteria were used: (1) a primary clinical diagnosis of a psychiatric disorder other than one of the anxiety disorders described above; and (2) not being fluent in Dutch since language problems would harm the validity and reliability of the data collected. However, during the intake phase in clinical practice at both of the participating treatment centres, patients who were also found to suffer from severe mental conditions such as psychotic disorder, bipolar disorder or severe addiction disorder, were directly referred for specialised treatment outside the anxiety disorder treatment unit and were thereby automatically excluded from participation in the study. When a comorbid personality disorder was also present, only the presence of a borderline personality disorder was reason to directly refer the patient for specialised treatment outside the anxiety disorder treatment unit.

4.2.4. Content of the anxiety disorder treatment guidelines

The Dutch treatment guidelines for patients with panic disorder with or without agoraphobia, social anxiety disorder or generalized anxiety disorder resemble the NICE (National Institute for Health and Care Excellence) guidelines and the guidelines from the British Association for Psychopharmacology with respect to the medication algorithms [17], and were first published in 2003 and were last updated in 2012, with no major changes regarding the first recommended treatment steps for secondary care [18, 19]. Both psychotherapy (mainly cognitive behavioural therapy) and pharmacotherapy (mainly selective serotonin reuptake inhibitors or serotonergic tricyclic antidepressants) count as equally valid treatment options. The recommended psychotherapeutic treatment steps consist of cognitive therapy and behaviour therapy. In addition, applied relaxation is recommended for patients with panic disorder

or GAD who do not respond to cognitive-behavioural interventions. The first three treatment steps in pharmacotherapy consist of three types of antidepressants. The guidelines favour selective serotonin reuptake inhibitors (SSRIs) over tricyclic antidepressants (TCAs). If an SSRI proves to be insufficient, switching to a second SSRI is recommended before prescribing a TCA. However, for a patient suffering from GAD the prescription of venlafaxine or buspirone is recommended instead of a second SSRI and before switching to the TCA imipramine. In social phobia, the third pharmacological treatment step is the prescription of a benzodiazepine or monoamine oxidase inhibitor (MAOI) rather than a TCA.

At any moment during treatment, if after the recommended period of time a chosen treatment step yields insufficient results, the recommendation is to switch to another treatment step within the same treatment modality (psychotherapeutic or pharmacotherapeutic) or to switch to treatment with a recommended treatment step of the other treatment modality.

4.2.5. Interventions

Control condition: dissemination

In 2003, as part of a Dutch national strategy to promote the use of newly developed guidelines, it was made widely known to general practitioners and professionals working in specialised mental health care that treatment guidelines for anxiety disorders had been developed. A broad outline of the guidelines was presented in Dutch scientific journals for psychiatrists and psychologists. A website (www.ggzrichtlijnen.nlwww.ggzrichtlijnen.nl) served as a free database for professionals and patients and presented the scientific background, recommendations and algorithms of the guidelines. In addition, the guidelines were available as a printed booklet. In the control condition, the guidelines were only disseminated and no further implementation took place.

Intervention condition: implementation

In the intervention condition, in addition to the general dissemination process described above, the guidelines were implemented following the steps developed by Grol and Wensing [20]. Based on a diagnostic analysis of possible barriers to implementation, an implementation plan was designed on three levels: patient, professional and organisation. This plan comprised the following interventions: (i) re-organisation of care: after the general intake procedure, the treatment coordinator of the treatment centre –an experienced cognitive behaviour therapist- would see all patients allocated to the anxiety

disorder treatment centre at the start of their treatment. So, the treatment coordinator was made responsible for devising the treatment plan for all patients allocated to the unit instead of the intake professional. During a process of shared decision making, this treatment coordinator and the patient designed a treatment plan according to the guidelines before the start of treatment; (ii) development and distribution of instruction materials for patients (patient folders on the description of recommended care according to the guidelines, from which patients could choose their preferred type of treatment) and professionals (desktop versions of the guidelines summarizing recommended treatment steps and essential treatment ingredients; treatment folders containing the available recommended evidence-based psychological treatment manuals); (iii) organisation of three educational meetings at which the content of the guidelines were discussed, that taken together took up about 12 hours of time; (iv) training of professionals in the skills needed to perform treatment as suggested in the guidelines; and (v) on-going monitoring of guideline adherence. Regular patient evaluations were held in which treatment progress was discussed from the perspective of the guideline algorithms. Also, one year after the start of the implementation, 50 medical files were reviewed and feedback on team performance was given by presenting the scores on key process indicators, and further goals for improvement were communicated. The implementation process is described in detail elsewhere [10].

4.2.6. Measurements

Data collection took place between the beginning of 2005 and July 2009. The lag-time between dissemination of the guidelines and the actual start of the implementation in the intervention condition was two years. In the intervention condition after a year of preparations, directly after the first educational meeting, the first patient was included for participation in the study.

Adherence to the guidelines

A review of each participating patient's medical files established whether treatment had been delivered according to the guideline algorithms or not, yielding a proportion of patients in both settings that had been receiving recommended care that was classified according to the following labels: 'adherent', 'non-adherent' and 'inapplicable'. The medical files were reviewed by means of specially developed process indicators. These indicators were selected by consensus by senior professionals from the Dutch Knowledge Centre for Anxiety and Depressive Disorders (www.nedkad.nl) [10, 21]. The selected

indicators coincided with the first two or three steps of the psychotherapeutic and pharmacotherapeutic branches of the treatment algorithms for the various anxiety disorders and measured whether these treatment steps had been followed adequately. For each patient, only the first year of treatment was assessed because all recommended treatment steps that were measured should have been applied during this first year, if indicated.

The adequacy of psychotherapeutic treatment steps was assessed by: (i) the delivery of the correct type of treatment; (ii) the presence of a treatment rationale; (iii) the assignment of homework; and (iv) the minimum recommended number of treatment sessions. In the same vein, the adequacy of pharmacological treatment steps was assessed by: (i) the prescription of the correct category and type of drug; (ii) prescription of the correct dosage and (iii) the correct minimum duration of the medication before evaluation. The process indicator was scored positively, when all these assessments were fulfilled according to guideline recommendations. In cases when there was one or more negative assessment, the process indicator was scored negatively.

In addition, a specific recommendation could also be judged as 'inapplicable' in the following cases: (i) when the primary diagnosis was revised; (ii) when a patient refused a specific intervention; (iii) when another recommended form of treatment had just started; (iv) when a sufficient response to the treatment had already been achieved; (v) when severe and acute psychosocial problems, suicidality or comorbid substance dependence had to take priority; (vi) in the case of severe side effects or somatic contraindications in psychopharmacological treatment; and (vii) when patients dropped out of treatment prematurely, rendering it impossible for the professional to provide adequate care. In these cases the corresponding process indicator was not scored and was omitted from the evaluation of adherence to the guidelines treatment algorithms.

If an algorithm was followed correctly and all the necessary steps in the treatment had been taken, the case would receive the label 'adherent'. If a single necessary treatment step in the algorithm had not been properly applied, the case would receive the label 'non-adherent'. If none of the treatment steps appeared to be applicable, the case would receive the label 'inapplicable' overall.

Two different assessors reviewed the medical files of patients in both conditions. During the review of the medical files, a specially developed checklist was used to determine the scores on relevant process indicators. To calibrate the judgement of each assessor, in both conditions, 30% of the files were independently coded twice. Differences between the coding forms were resolved

by reviewing the original files, leading to one coding form per medical file. In cases where there was uncertainty about how to score a certain process indicator, consensus was reached through discussion with two other members of the study group (DBO and AvB). The same decision rules that were derived from this consensus process were applied to all other medical files. Because of the differential layout of the medical files, the assessors were not blind to the condition under which a patient belonged. However, they were blind for treatment outcome.

Patient outcomes
Patients were assessed at baseline and at 1-year and 2-year follow-ups with validated self-rating scales. The *primary outcome measure* was the mean difference from baseline of the Beck Anxiety Inventory total score (BAI; total score range 0-63 [22]). *Secondary outcome measures* were: (i) the percentage of patients responding and achieving remission on the BAI according to the criteria of Jacobson and Truax [21] after 1-year and 2-year follow-ups. *Response* was defined as the presence of reliable change (decrease > 10 points) on the BAI, while *remission* was defined as the presence of reliable change (decrease > 10 points) on the BAI plus an absolute BAI score < 11. This cut-off point was the calculated mean between the BAI score of the participants in the NESDA study [13] with or without an anxiety disorder.
(ii) presence and severity of phobic avoidance behaviour measured with the Fear Questionnaire (FQ; range 0 -120) [23]. (iii) co-morbid depressive symptoms measured with the Inventory of Depressive Symptoms (IDS; range 0-84) [24].

4.2.7. Sample size considerations

For sample size computations, we assumed that the effect of the implementation of the treatment guidelines for anxiety disorders on the BAI, the primary outcome measure, would have a medium effect size (Cohen's d=.5). In a randomised controlled trial the number of patients required to obtain a power of .80 to detect a medium effect size is 42 per condition for longitudinal data analysis having three measurements and assuming a correlation coefficient of the repeated measures of .3 and alpha=.05 [25]. Since the respondents in the current study were not randomly allocated, we wanted to at least be able to use statistical techniques that allowed us to control for differences in patient characteristics that may affect the score on the BAI; i.e. to control for confounding

bias, which cost some power. Therefore the aim was to include at least 84 respondents per condition.

4.2.8. Statistical methods

Standard descriptive statistics were used to describe the study population. To check whether patients in the two conditions differed, t-tests for continuous variables and χ^2 tests for proportions were used. Difference in guideline adherence between the two treatment centres was analysed with χ^2 or Fisher exact tests.

The effect of systematic guideline implementation on the continuous outcome measures of the study was analysed with mixed-effects linear models that use all available information of the intention-to-treat sample. The random-intercept model included measurement (baseline, 1-year and 2-year follow-up), condition (intervention vs. control condition) and the measurement-by-condition interaction as fixed effects and patients (first level) as random effects. The effectiveness of implementing the guidelines was studied using the entire group of patients originally included in the study (divided into adherent, non-adherent cases and cases in which the guidelines were judged to be inapplicable).

Due to the observational nature of the design of the study, differences in baseline characteristics of patients in the intervention and control conditions were expected to exist. Out of methodological considerations, we chose to primarily investigate raw change scores to detect longitudinal changes on the dependent outcome variables and not to correct for possible differences in baseline symptom severity. Research has shown that the inclusion of such baseline covariates in linear models will have only a slight impact on the inferences for longitudinal effects [26]. However, because correction for baseline differences is common practice, the same data was also analysed using residual change scores, thus correcting for baseline differences on the dependent variables. Since both types of analyses yielded the same results, only the results of the mixed-model approach using the raw changes scores are reported.

To rule out possible bias through confounding by factors other than baseline symptom severity, the variables of age, gender, national origin, educational level, and number of treatment sessions received during the first year were added to the regression analysis, in a step-by-step fashion. If adding one of these variables led to a 10% change in the estimation of the effect of measurement-by-condition interaction, this variable was designated as a relevant confounder. However, none of these variables appeared to confound the

relationship between the central independent variable and the dependent outcome variables.

To study further whether the difference in treatment outcome between the two study conditions could be related to the difference in guideline adherence, a second set of multilevel linear regression analyses were performed post hoc, using a model that regressed the measurement-by-guideline adherence interaction on measurement (baseline, 1-year and 2-year follow-up) and guideline adherence (yes/no) as fixed effects and patients (first level) as random effects.

We calculated within group pre-post effect sizes by dividing the differences of follow-up and baseline means by baseline standard deviations. We calculated between group pre-post effect sizes by dividing the between group (experimental vs. control) differences of pre-post differences by the pooled (experimental and control group) baseline standard deviation and using a bias adjustment factor (see d-ppc2 in Morris, 2007) [27].

All tests of treatment effects were conducted at a two-sided alpha level of 0.05. All basic statistical calculations in this study were performed with SPSS, version 17.0 (SPSS Inc., Chicago IL, US). The multilevel linear regression analyses were performed using Stata 12.1 (Stata Corp., College Station TX, US).

4.3. Results

4.3.1. Patient inclusion and attrition rates

The study flow diagram (Figure 1) shows participant recruitment, the number of patients that were finally included for analysis in the intervention and the control condition and retention at 1-year follow-up and 2-year follow-ups. Of 106 patients assigned to the intervention condition, having a primary diagnosis of panic disorder with or without agoraphobia, social phobia or generalized anxiety disorder and providing written informed consent, diagnosis was confirmed in 90.6% (n=96) by an independent assessor using the CIDI [15]. Ten patients with no CIDI-confirmed anxiety disorder diagnosis were excluded. These did not differ significantly in their BAI, FQ and IDS baseline scores from the patients who were included in the study. Of 108 patients assigned to the control condition, 23.1% (n=25) has incomplete medical records. These patients were excluded from the analyses and did not significantly differ in their BAI, FQ and IDS baseline scores from the included patients. Two patients who did not return their baseline questionnaires were also excluded from further analyses.

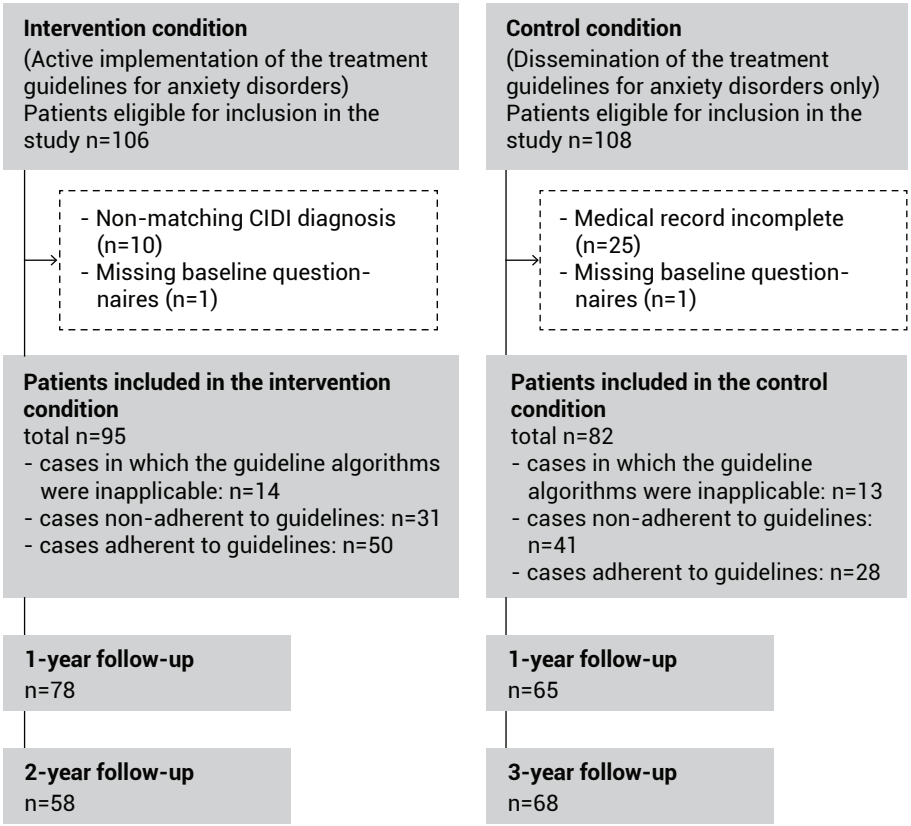

Figure 1. Diagram showing flow of participants through the implementation study

Demographic characteristics and clinical status variables at baseline and the number of treatment contacts received within the first year of treatment for patients in the intervention and control conditions are shown in Table 1. As follows from this table, patients from the intervention condition had significantly less education and scored significantly higher on BAI and FQ, suggesting that there were more severe anxiety and avoidance symptoms in the intervention condition.

Data on primary outcome measures were obtained from 143/177 (80.8%) of the total number of patients at 1-year follow-up and 126/177 (71.2%) at 2-year follow-up (Figure 1). Data dropout was significantly greater at 2-year follow-up in the intervention condition (38.9%) vs. the control condition (17.1%;χ^2(df=1)=10.27;p=.001). Data completers did not differ significantly from data dropouts on the baseline variables presented in Table 1, except that they

Table 1. Comparison of demographic and clinical status variables at baseline, and number of received treatment contacts of patients included in the intervention and control conditions

	Intervention condition (n=95)		Control condition (n=82)		p-value
Age: Mean (SD)	34.06	(11.7)	35.90	(10.7)	.281
Gender (female): n (%)	52	(54.7)	54	(65.9)	.132
Northern European ancestry: n (%)	84	(89.4)	73	(89.0)	.943
Having no partner: n (%)	43	(45.3)	34	(41.5)	.611
Education in years: Mean (SD)	10.07	(2.3)	12.95	(3.4)	<.001 **
Main diagnosis panic disorder: n (%)	55	(57.9)	45	(54.9)	.686
Main diagnosis social phobia: n (%)	28	(29.5)	24	(29.3)	.976
Main diagnosis GAD: n (%)	12	(12.6)	13	(15.9)	.539
BAI Mean (SD)	24.28	(12.9)	20.29	(11.3)	.031 *
FQ Mean (SD)	48.35	(24.6)	35.13	(18.7)	<.001 **
IDS Mean (SD)	28.35	(12.9)	26.46	(11.1)	.306
Number of treatment contacts within the first year of treatment	17.38	(13.9)	15.93	(10.4)	.442

SD = Standard Deviation; GAD= generalized anxiety disorder; BAI = Beck Anxiety Inventory; FQ = Fear Questionnaire; IDS = Inventory of Depressive Symptoms

** significant difference p<.001, * significant difference p<.05

had significantly less education (number of years of education: Mean 11.8 vs. 10.8; t=2.22;df=153.9;p=.028).

4.3.2. Adherence to guidelines and long-term health care usage

The guideline algorithms proved to be inapplicable to 14/95 (14.7%) of the patients in the intervention condition vs. 13/82 (15.9%) of the patients in the control condition (χ^2=0.42;p=.837), leaving 81 patients and 69 patients respectively for whom the guidelines could be considered applicable. The most important reasons why the guidelines proved to be inapplicable were (in order of frequency): (i) revision of the primary diagnosis shortly after start of treatment; (ii) the patient dropped out shortly after start of treatment, which made it impossible to carry out proper care; (iii) acute crisis situations, or serious psychosocial problems, which required urgent attention and made it impossible to apply any of the guideline recommendations.

In 50/81 (61.7%) of the cases in the intervention condition, treatment was adherent to the treatment guidelines vs. 28/69 (40.6%) of the cases in the control

condition (χ^2(df=1)=6.68;p=.01). Table 2 presents adherence rates to the different recommended treatment steps, which help explain the greater adherence rate to the guidelines' algorithms in the intervention condition when compared to the control condition. The results suggest that the difference can mainly be attributed to the number of patients who received adequate cognitive therapy. Although many patients in the control condition received cognitive therapy this process indicator was frequently scored negatively because no adequate homework assignments were given or the duration of treatment was too short.

At 2-year follow-up, patients were asked whether they had received treatment contacts for secondary mental health care during the past half year. Patients from the control condition 55/72 (76.4%) vs. 25/56 (44.6%) from the intervention condition reported they had had such treatment contacts within this time period (χ^2(df=1)=13.54; p<.001).

4.3.3. Outcome on clinical ratings

Table 3 depicts the predicted means and SDs on the BAI, FQ and IDS of patients in the intervention condition (n=95) and control condition (n=82), derived from multilevel linear regression analyses conducted on the intention-to-treat sample.

Primary outcome measure: Compared to the control condition, the decrease in anxiety symptoms from baseline to 1-year follow-up on the BAI was 4.1 points larger in the intervention condition (95%CI: 0.84-7.34;p<.05;*d*=.45). The decrease in anxiety symptoms from baseline to 2-year follow-up yielded a non-significant difference of 3.0 points on the BAI in favour of the intervention condition (95%CI -0.35-6.44;p=.08;*d*=.36).

Secondary outcome measures: Compared to the control condition, the percentage of patients responding at 1-year follow-up was significantly higher in the intervention condition (52.6% vs. 33.8%; χ^2(df=1)=5.04;p=.025). The percentage of patients achieving remission at 1-year follow-up was also significantly higher in the intervention condition (33.3% vs.16.9%; χ^2(df=1)=4.98;p=.026). At 2-year follow-up these significant differences disappeared: the percentage of responders in the intervention condition was 48.3% vs. 44.1% in the control condition; χ^2(df=1)=.22;p=.641 and the percentage of patients achieving remission in the intervention condition was 32.8% vs. 29.4% in the control condition; χ^2(df=1)=.16;p=.685.

Phobic avoidance behaviour (FQ): at 1-year follow-up improvement in the intervention condition was 5.6 points greater than the improvement in the

Table 2. Adherence to the different recommended treatment steps

Guideline recommendation	Intervention condition		Control condition		Difference in percentage receiving treatment as indicated	p-value
Number of patients indicated for cognitive intervention and the percentage that actually received it	71	77.5%	54	59.3%	18.2%	p=.028*
Number of patients indicated for exposure intervention and the percentage that actually received it	16	50%	36	41.7%	8.3%	p=.577
Number of patients indicated for medication step 1 and the percentage that actually received it	24	66.7%	32	71.9%	5.2%	p=.675
Number of patients indicated for medication step 2 and the percentage that actually received it	9	44.4%	9	44.4%	0.0%	p=.999
Number of patients indicated for medication step 3 and the percentage that actually received it	5	40.0%	8	25.0%	15.0%	p=.999

* significant difference p<.05

control condition (95%CI 0.10-11.02;p<.05;*d*=.34). At 2-year follow-up this difference was 11.0 points greater in the intervention condition (95%CI 5.27-16.74;p<.05;*d*=.68).

Co-morbid depressive symptoms (IDS): No significant differences between the two conditions were observed for IDS at 1- and 2-year follow-ups. At 1-year follow-up the decrease was 2.26 points greater in patients in the intervention condition (95%CI -0.95-5.48;p=.167;*d*=.26), while at 2-year follow-up a small difference of 1.3 points more in the intervention condition was found (95%CI -2.05-4.69;p=.441;*d*=.15).

4.3.4. Guideline adherence and treatment outcomes

To further study whether the differences in treatment outcome between the two study conditions were critically dependent on differences in guideline adherence, a second set of multilevel linear regression analyses were performed post hoc, using all patients from both intervention and control condition. First,

Table 3. Predicted Means and Standard Deviations (SD) on the BAI, FQ and IDS of patients in the intervention condition (n=95) vs. the control condition (n=82), at baseline, the 1- and 2-year follow-ups, based on multilevel linear regression analysis in the intention-to-treat sample

		Baseline	1-year follow-up		2-year follow-up	
		Mean (SD)	Mean (SD)	ES	Mean (SD)	ES
BAI	Intervention condition	24.3 (8.1) [a]	14.1 (8.6) [b]	1.3	12.9 (9.4) [c]	1.4
	Control condition	20.3 (8.7)	14.2 (9.3)	0.7	12.0 (9.2)	1.0
FQ	Intervention condition	47.6 (15.8) [d]	33.0 (16.1) [b]	0.9	28.5 (17.3) [e]	1.2
	Control condition	35.1 (16.5)	26.1 (17.4)	0.5	27.1 (17.3)	0.5
IDS	Intervention condition	28.3 (8.4)	18.4 (8.8)	1.2	17.8 (9.6)	1.3
	Control condition	26.5 (9.0)	18.8 (9.6)	0.9	17.3 (9.4)	1.0

SD = Standard Deviation; ES = (baseline to follow-up) Effect Size; BAI = Beck Anxiety Inventory; FQ = Fear Questionnaire; IDS = Inventory of Depressive Symptoms
[a] Baseline intervention vs. control condition p<0.05
[b] Pretest - 1-year follow-up improvement intervention vs. control condition p<0.05
[c] Pretest - 2-year follow-up improvement intervention vs. control condition p<0.10
[d] Baseline intervention vs. control condition p<0.001
[e] Pretest - 2-year follow-up improvement intervention vs. control condition p<0.001

a check was made whether patients whose treatment did adhere (n=78) and patients whose treatment did not adhere to the guidelines (n=72) differed critically from another in terms of certain patient characteristics, which could influence treatment results. With respect to all variables as also mentioned in table 1, patients whose treatment did adhere to the guidelines significantly differed from the group of patients whose treatment did not, only in terms of the following three aspects: the percentage of patients being single (32.1% vs. 50.0%;χ^2(df=1)=4.99;p=.025); educational level (number of years of education: Mean 11.1 vs. 12.2;t=2.13;df=148;p=.035), and; the percentage of patients diagnosed with panic disorder (64.1% vs. 45.8%;χ^2(df=1)=5.06;p=.025). None of these variables were found to be significantly related to treatment outcome, indicating that they did not confound the relationship of guideline (non)-adherence and treatment outcome. Multilevel linear regression analyses were performed on BAI, FQ and IDS, using a model that regressed the measurement-by-guideline adherence interaction on measurement (baseline, 1-year and 2-year follow-up) and guideline adherence (yes/no) as fixed effects and patients (first level) as random effects. The outcome is presented in Table 4. The data suggest that on all three measurements after 1-year and 2-year follow-

ups adherent treatments yielded superior results compared to non-adherent treatments with medium between group effect sizes.

Table 4. Predicted Means and Standard Deviations (SD) on the BAI, FQ and IDS of treatments adherent (n=78) vs. non-adherent to the anxiety disorders guidelines algorithms (n=72), at baseline, the 1- and 2-year follow-ups, based on multilevel linear regression analysis

		Baseline	1-year follow-up		2-year follow-up	
		Mean (SD)	Mean (SD)	ES	Mean (SD)	ES
BAI	Adherent	21.3 (8.3)	10.3 (8.8) [a]	1.3	8.9 (9.2) [b]	1.5
	Non-adherent	22.6 (8.6)	17.3 (9.1)	0.6	15.3 (9.1)	0.8
FQ	Adherent	37.5 (15.3) [c]	21.7 (16.0) [d]	1.0	21.0 (16.6) [e]	1.1
	Non-adherent	43.9 (15.8)	36.2 (16.4)	0.5	34.4 (16.6)	0.6
IDS	Adherent	25.3 (8.3)	14.5 (8.8) [f]	1.3	13.3 (9.3) [b]	1.4
	Non-adherent	28.5 (8.7)	21.2 (9.1)	0.8	21.2 (9.2)	0.8

SD = Standard Deviation; ES = (baseline to follow-up) Effect Size; BAI = Beck Anxiety Inventory; FQ = Fear Questionnaire; IDS = Inventory of Depressive Symptoms
[a] Baseline - 1-year follow-up improvement adherence vs. no adherence $p<0.001$
[b] Baseline - 2-year follow-up improvement adherence vs. no adherence $p<0.01$
[c] Baseline adherence vs. no adherence $p<0.10$
[d] Baseline - 1-year follow-up improvement adherence vs. no adherence $p<0.01$
[e] Baseline - 2-year follow-up improvement adherence vs. no adherence $p<0.05$
[f] Baseline - 1-year follow-up improvement adherence vs. no adherence $p<0.05$

4.4. Discussion

In this study guideline adherence rates and treatment outcomes between two treatment centres for anxiety disorders were compared. The guidelines were implemented in one of these centres (the intervention condition). In the control condition, the guidelines were only disseminated. Guideline adherence rates, as measured during the first year of each patient's treatment, were found to be significantly higher in the intervention condition. Patients in this condition also showed superior treatment gains on anxiety and avoidance symptoms at the 1-year follow-up. At the 2-year follow-up, however, the difference on anxiety symptoms between the two conditions was not significant, while the difference on avoidance symptoms remained.

Since a significantly larger percentage of patients in the control condition continued treatment during the second treatment year, treatment gain in the control condition measured as the decrease in anxiety symptoms from baseline to 2-year follow-up improved relative to the intervention condition. This where the decrease in avoidance behaviour as measured from baseline to 2-year follow-up still remained greater in the intervention condition. Overall the data suggest that the implementation of guidelines leads to somewhat greater treatment gains with respect to anxiety symptomatology. Moreover, treatments which were adherent to the guidelines were shorter, indicating that the care was more efficient.

We could demonstrate in both conditions that adherent treatments yielded superior outcomes than non-adherent treatments. It is thus plausible that the difference in outcome found between the two conditions could be attributed to the difference in adherence. Indeed, except for guideline adherence, the conditions did not differ very much with respect to the composition of professionals working in both treatment settings. Unfortunately however, the patients included in the intervention condition had more severe scores on anxiety outcome variables than those in the control condition. For methodological considerations we initially choose not to correct for baseline differences in symptom severity in our analyses [26]. All the analyses were repeated, correcting for baseline differences by using residual change scores, which did not critically affect our results.

There are some limitations to this study that have to be recognised however. First, because of the non-randomised nature of the 'double cohort' study design, we had to take into account the chance that our findings might be influenced by confounders. We therefore investigated many putative confounding variables, also in addition to baseline symptom severity. None of these appeared to be a relevant confounder, providing assurance that the observed effect may indeed be an effect caused by the difference in implementation between the two conditions. Second, a point of criticism is the use of patient files as a source of information when determining guideline adherence. This method of data collection was chosen because it is rather easy to carry out. In addition, because in both centres the professionals were not aware of this evaluation type, we excluded what is known as the 'Hawthorne effect'. Had we used audio or video tapes of treatment sessions, the content of these sessions could possibly have been compromised by the fact that the professional would exhibit behaviour thought to be more 'desirable' because he/she felt under scientific scrutiny.

The methodological strengths of our study include the use of two well-diagnosed, representative clinical cohorts of secondary mental health care patients with anxiety disorders. We included 'real-life' patients because we applied only one exclusion criterion (insufficient proficiency in the Dutch language), enhancing the external validity of our study results.

The present study showed that there is room for improvement in dissemination, a typical strategy for the implementation of guidelines, in order to enhance quality of care and outcomes at the patient level. Implementation, in addition to dissemination, yielded superior performance with regard to adherence levels and treatment results in a 2-year period and especially in the short run, with small to medium between-group effect sizes on the anxiety disorder-specific outcome measures. The results also make clear however, that quite a number of patients fail to show sufficient treatment response when treated in a specialized treatment setting in which evidence-based guidelines are implemented. Since implementing guidelines is a continuous process, the expectation is that more time and efforts spend on implementing the guidelines, could have further improved adherence levels and treatment outcomes. With the effectiveness of current evidence-based treatment options however, even in patients receiving 100% guideline concordant care, not every patient is expected to show remittance. A recent published study shows that at this time it is hard to predict which anxiety disorder patients will or will not profit from guideline-adherent treatment in terms of demonstrating adequate treatment response [28]. Efficiency of healthcare for patients with an anxiety disorder, could be greatly improved if one would be better able to predict in advance which patients will or will not benefit from a certain type of treatment. More research is needed to allow for such personalized medicine in line with directions which are for example given for the treatment of unipolar depression [29], These directions help to guide the patient to the treatment method with the highest chance of success. Notwithstanding, the present results do suggest that the systematic implementation of available practice guidelines may improve quality of care, and therefore should encourage more widespread initiatives aimed at the systematic implementation of guidelines in mental health care.

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Declaration of interest

MKvD, DBO, AWH and BWJHP declare to have no conflicts of interests at all: there has been no payment received for participation in meetings or advisory boards, nor for research conduct from pharmaceutical companies or other private enterprises by these authors. MJPMV declares he has received funding from Eli Lilly in 1991 and 1996 for two trials in which he was co-investigator, he has not received any payment for participation in meetings or advisory boards. AJLMvB declares the following conflicts of interests: there has been no payment received for participation in advisory boards nor for other private enterprises. Unrestricted educational grants have been given by Lundbeck (development of post-graduate course for psychiatrists), Servier (evaluation of agomelatine in panic disorder) and Glaxo SmithKline (writing text on DSM-5 changes in anxiety disorders).The statistical analyses for this study were largely carried out by AWH; further details about the procedures carried out for the statistical analyses, can be obtained by email: a.hoogendoorn@ggzingeest.nl.

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Chapter 5

Predictors of non-response and persistent functional impairments in treatment adhering to evidence-based practice guidelines for anxiety disorders

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Abstract

Background: Several countries have developed guidelines for anxiety disorders containing algorithms that summarize the recommended treatment steps for these disorders. It is important to know which patients have a poor prognosis for treatment according to such algorithms.

Aims: To investigate the predictive power of variables known to be able to influence treatment prognosis in situations where practice guidelines for anxiety disorders are adhered to.

Method: To study the predictive power of variables that are known to be able to influence treatment prognosis, 81 patients who participated in a guideline implementation study and whose treatment was found to adhere to available guidelines were selected. Using logistic regression analysis two models were constructed: one to predict treatment non-response; another to predict persistent functional impairments at the 1-year follow-up.

Results: The final prediction model for treatment non-response contains only gender and secondary gain variables. It appears that: males have a higher likelihood (p=.074), and patients that report hopes of obtaining external benefits by seeking treatment have a lower likelihood (p=.054) of showing treatment non-response at the 1-year follow-up. The discriminatory power of this model was found to be poor, however. The model for persistent functional impairments includes gender, satisfaction with the accessibility of healthcare services and the presence of a comorbid anxiety disorder. It appears that: males (p=.087) and patients who express dissatisfaction with the accessibility of care (p=.008) have a higher likelihood, and that; patients who suffer from an additional comorbid anxiety disorder have a lower likelihood (p=.079) of persistent functional impairments. The discriminatory power of this model is excellent.

Conclusion: It remains difficult to predict which anxiety disorder patients will not benefit from treatment that is tailored according to available practice guideline recommendations, therefore no one should be prevented from being offered such treatment, if one removes barriers in attending treatment.

5.1. Introduction

A recent cohort study carried out among outpatients in a mental health care setting showed that outpatients suffering from an anxiety disorder whose treatment adhered to the available clinical-practice guidelines had greater symptom reduction after one year, compared to patients whose treatment did not adhere to these guidelines [1]. However, some patients remain non-responsive to treatment, even when their treatment was found to adhere to the guidelines and despite the fact that they were able to receive multiple recommended evidence-based treatments. The ability to identify such patients before treatment begins is an important challenge in clinical practice. The ability to do so could lead to improvement of the guidelines at a more individualized level, which would directly benefit patients.

Recently Taylor and colleagues [2] provided an overview of what is known about factors that influence non-adherence and non-response in anxiety disorder patients receiving either antidepressant medication or cognitive-behavioural interventions. Based on the existing literature, they suggest that factors relevant to predicting treatment outcome include: low treatment motivation, hidden secondary motives for seeking treatment, encountering barriers that hamper treatment attendance (e.g. transportation problems or difficulties arranging for childcare), pre-treatment symptom severity and the presence and severity of possible comorbid psychopathology [2]. Many of these factors have been investigated as part of intervention studies examining the effects of monotherapies. In these studies patients were randomly allocated to an experimental condition or a control condition. Therefore patients lacked the opportunity to select a treatment of their own choice. This may adversely affect the generalizability of the findings to daily practice. None of the studies mentioned by Taylor et al. [2] investigated the influence of all of the above-mentioned factors, in concert, on treatment outcome. Thus, the question of what the predictive power of these prognostic factors, alone or in combination, would be on the treatment outcome for the patient is still operative.

A systematic review of the prognostic factors of long term disability in mental disorders performed by Cornelius et al. [3] sheds light on some additional factors. In this review strong evidence was found for age as a relevant factor for continuous disability. Limited evidence was found for gender, education, unemployment, and socioeconomic status in general. Also, a patient's cultural background should be considered an additional putative factor predicting non-response and continuous disability, especially because of established

higher drop-out rates from general mental health treatment for ethnic minorities in the Netherlands [4].

The aim of the present study is to investigate the predictive value of the factors described above in predicting non-response and long-term disability. In the present study these factors will be explicitly studied in conjunction with one another. The context of this study is an outpatient clinical setting where treatment is optimized according to the available evidence-based treatment guidelines, and where patients were encouraged to choose their own preferred methods of treatment.

5.2. Method

5.2.1. Study participants and procedure

The present study used data collected as part of a study that investigated the feasibility and effectiveness of adhering to clinical-practice guidelines for anxiety disorders in secondary mental health care [1, 5]. This study was approved by the medical ethics committee of the VU University Medical Centre Amsterdam. Detailed information about study design and measurement procedures can be found in the two aforementioned references. A general description of the relevant research procedures is given here.

A cohort for the study was formed of patients who were registered at the community mental health care centre in Almelo, the Netherlands, after the implementation of the Dutch multidisciplinary practice guidelines for anxiety disorders was begun [5, 1]. For the present study we included patients aged 18 years or older who i) were diagnosed with a primary DSM-IV diagnosis of panic disorder with/without agoraphobia, social phobia, obsessive compulsive disorder (OCD), generalized anxiety disorder (GAD), posttraumatic stress disorder (PTSD), specific phobia or hypochondriasis; ii) gave written informed consent for participation, and iii) received treatment according to the Dutch anxiety disorder guidelines recommendations (see: www.ggzrichtlijnen.nl). Co-morbidity with other mental disorders was allowed.

In order to maintain representativeness, only two exclusion criteria were used for the current study: (1) a primary clinical diagnosis of a psychiatric disorder other than one of the anxiety disorders described above; and (2) not being fluent in Dutch since language difficulties would harm the validity and reliability of the data collected.

5.2.2. Investigated practice guidelines and measure of adequate guideline adherence

The Dutch multidisciplinary guidelines for anxiety disorders contain recommendations for both psychotherapy (mainly cognitive behavioural therapy, but also EMDR for PTSD) and pharmacotherapy (mainly selective serotonin reuptake inhibitors or serotonergic tricyclic antidepressants). These options are counted as equally valid.

A review of each participating patient's medical file was used to establish whether treatment had actually been delivered according to the guideline algorithms, originally yielding a proportion of patients who had been receiving recommended care that was classified according to the following labels: "adherent", "non-adherent" and "inapplicable" [1]. The medical files were reviewed by specially developed process indicators. A checklist was used to score the different indicators [5]. Ultimately, if an algorithm was followed correctly and all the necessary steps in the treatment had been taken, the case would receive the label "adherent." If a single necessary treatment step in the algorithm had not been properly applied because of a failure on the part of the responsible health care provider, the case would receive the label "non-adherent." If none of the treatment steps appeared to be applicable, the case would receive the label 'inapplicable' overall. For the present study only the 'adherent' cases were included for further analyses [1]. Measurements relevant to treatment outcome were performed at baseline and at a 1-year follow-up.

5.2.3. Outcome measures

We sought to construct two models to predict non-response with respect to clinical symptoms and to functional limitations. (i) Clinical symptoms were measured with the Symptom Checklist (SCL-90-R) [6, 7]. A patient's overall score on the SCL-90-R reflects his or her general level of psychopathology (range 0–360). Non-response was operationalized as not showing reliable change on the SCL90-R total score from baseline to 1-year follow-up, according to the Reliable Change Index (RCI) criteria defined by Jacobson and Truax [8]. Applied to the SCL90-R total score, this means that reliable change on the SCL-90-R is indicated by a score of at least 30 points. Thus, all cases with a change score of less than 30 points were defined as non-responders. (ii) To assess functional impairments at baseline and at the 1-year follow-up the Sheehan Disability Scale (SDS) [9] was used. This patient-rated measure asks the subject to rate on a scale ranging from 1 ("not at all") to 10 ("extremely"): 1) the extent to which symptoms have disrupted work / school work; 2) the

extent to which symptoms have disrupted social life/leisure activities, and 3) the extent to which symptoms have disrupted family life/home responsibilities. The sum of the scores on these three subscales yields the SDS total score (range 3 to 30), and provides a general impression of the level of functional impairment experienced by the patient. The persistence of functional impairment was also defined dichotomously. A patient with an SDS total score of 6 or higher at the 1-year follow-up was considered to suffer from persistent functional impairments. In the literature on anxiety disorders an SDS total score of 5 or less has been used to signal functional recovery [10, 11].

5.2.4. Predictors

Demographic variables

The patients' gender and age were derived from the medical files. Patients were asked to report their country of birth and also the birth countries of both of their parents, their educational level, employment status and monthly net income. In the present study a patient is considered to have a foreign background if at least one of his or her parents was born outside the Netherlands or its former colonies. Ultimately, the patients' educational level was operationalized dichotomously, as having completed only primary education (yes/no). This where the level of education in the cohort of patients studied was already relatively low on average. It was hypothesized that reaching adequate treatment effect when adhering to the guidelines, would be especially challenging in patients that only finished elementary school at best.

Assessment of DSM-IV axis I disorders

The presence of a DSM-IV axis I disorder was assessed by the Mini International Neuropsychiatric Interview (M.I.N.I.) [12, 13], administered by a trained clinician as part of the standardized intake procedure at the community mental health care center. In patients with co-morbid mental disorders the primary diagnosis was defined as the psychiatric disorder associated by the patient with the greatest degree of suffering. In determining the influence on treatment outcome and persistent functional impairments, the presence of a comorbid secondary anxiety disorder, and the influence of a comorbid depressive disorder were separately investigated.

Psychiatric status variables

The Personality Diagnostic Questionnaire-4+ was used as a screener for the presence of comorbid DSM-IV axis II personality disorders, at baseline [14,

15]. The PDQ4+ is a self-administered, true/false screening questionnaire. The PDQ4+ total score, the sum of the scores of the individual items, can be used as an index of overall personality disturbance (range 0-99), with a total score of 30 or higher indicating a substantial likelihood that the subject has a significant personality disturbance [16]. This 30 point cut-off value was used as a dichotomous measure for the absence or presence of personality disturbance.

To assess patient motivation the Nijmegen Motivation List 2 (NML2) was administered at baseline [17]. Only the preparedness subscale (range: 10 to 60) of the NML2, which consists of 10 items that express the patient's preparedness to actively invest in treatment and to make sacrifices for the sake of treatment, was investigated for its predictive value on treatment outcome. Research has shown this NML2 subscale to be the most significantly related to treatment outcome in outpatient mental health care of the subscales in the NML2 [17].

Secondary gain was operationalized in accordance with the DSM-IV definition of "obtaining external benefit" [18; p. 453]. Patients were explicitly asked to indicate whether special support and mediation by therapists was expected (yes/no) and the aspects for which they expected support and mediation. Patients could tick the following items, where appropriate: job, social security claims, budget for getting help from relatives, financial problems, compensation for unusual healthcare costs, legal/police matters, accommodation, insurance, other.

To assess practical barriers that could hamper treatment attendance the item from the Dutch version of the World Health Organization Quality Of Life questionnaire (WHOQOL- BREF) [19] was used and administered at baseline. This item asks the patient to rate on a scale ranging from 1 ("very dissatisfied") to 7 ("very satisfied"), their degree of satisfaction with the accessibility of the health services. In order to facilitate interpretation, ultimately this variable was also dichotomized. Scores ranging from 1 to 4 were recoded to 1, indicating that the patient was less than satisfied with the accessibility of the healthcare services. Scores 5 to 7 were recoded to 0, indicating that the patient was satisfied or very satisfied with the accessibility of the health services used.

5.2.5. Statistical analyses

Standard descriptive statistics were used to describe the study population. To check whether attrition bias posed a threat to the validity of the study results differences between study completers and study drop-outs, t-tests for continuous variables and χ^2 tests for proportions were used on the original (i.e. non-imputed) data. Ultimately, missing data resulting from patients dropping

out of the study were handled by using multiple imputation by chained equations (MICE), which operates under the assumption that given the variables used in the imputation procedure, the missing data are Missing At Random (MAR). There were three sets of variables selected for the imputation model [20]: all variables that appeared in the complete data model, all variables that related to dropping out of the study, and all variables that related to the two main outcome variables (the severity of psychiatric symptoms (SCL-90-R) at follow-up measurement and the score for functional impairment (the Sheehan Disability Scale). Data imputations were performed with chained equations method in Stata 12.1 using predictive mean matching (PMM) as the imputation method with 20 imputations.

All final analyses were carried out on the multiple imputed data set, using all cases originally included in the study that were judged to have been adequately treated according to the guideline algorithms (guideline adherent; n=81). In constructing a prediction model for "non-response" and "functional impairment" we used a model-building strategy called "purposeful selection of covariates" [21]. After a careful bivariate analysis of each independent variable, retaining any variable whose bivariate test has a significance level below 0.25 (step 1), a multivariate model is fitted (step 2) retaining all variables with significance levels below 0.10, checking that none of the coefficients changed markedly in magnitude (i.e. $\Delta\hat{\beta} > 20\%$) and re-entering a predictor if necessary in order to prevent such a change (step 3), and finally evaluating the possible addition of each independent variable individually (step 4). Non-linearity (step 5) and interaction effects (step 6) are evaluated, and ultimately the "final model" obtained is evaluated in terms of model fit by pseudo R-square and "area under the receiver operating characteristic (ROC) curve" (step 7).

The basic statistical calculations in this study were performed with SPSS, version 17.0 (SPSS Inc., Chicago IL, US). The multiple imputations and analyses using logistic regression on the imputed data were performed using Stata 12.1 (Stata Corp., College Station TX, US).

5.3. Results

As can be seen from the flowchart (Fig. 1), 81 patients from the group initially included in the study were recommended for treatment according to the treatment guidelines and were judged to have received such treatment (guide-

line adherent cases). The attrition rate of patients in this group at the 1-year follow-up was 16%.

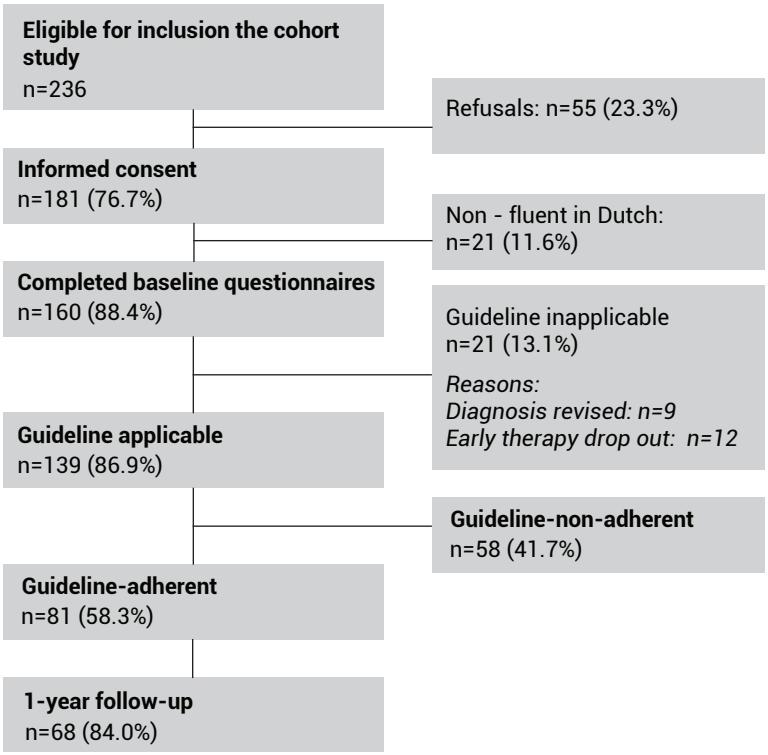

Figure 1. Flow chart for patient inclusion

Tables 1 and 2 present demographic and clinical characteristics, respectively, of the 81 adherent cases and characteristics of the study completers vs. patients lost to follow-up.

As shown in tables 1 and 2, the proportion of males was higher in the group of patients who were lost to follow-up compared with the study completers. Furthermore, patients lost to follow-up were less educated than study completers and were less motivated to complete treatment. Moreover, somewhat more patients lost to follow-up were diagnosed with a social phobia.

At the 1-year follow-up the estimated overall percentage of non-responders on the SCL-90-R among patients whose treatment adhered to the guidelines was 40%, while 63% experienced persistent functional impairments.

Table 1. General characteristics of the study sample of completers and patients lost to follow-up (original data)

	Total Sample (n=81)		Study completers (n=68)		Patients lost to follow-up (n=13)		P-values between group differences: Study completers vs. Patients lost to follow-up
Age: Mean (SD)	33.5	(11.9)	33.49	(11.4)	33.62	(15.2)	.972
Gender (male): n (%)	29	(33.8)	20	(29.3)	9	(69.2)	.006 **
Foreign background (yes): n (%)	11	(13.6)	8	(11.8)	3	(23.1)	.275
Educational level; only primary school or less: n (%)	11	(13.6)	7	(10.3)	4	(30.8)	.048 *
Unemployed (yes): n (%) Missing item values: n	38 1[a]	(46.9)	30 1[a]	(44.8)	8 0[a]	(61.5)	.268
Net monthly income in Euros: mean (SD) Missing item values: n	877.4 19[a]	(602.7)	914.3 18[a]	(611.4)	723.4 1[a]	(562.8)	.329
NML2 preparedness score: mean (SD)	47.4	(8.1)	48.2	(7.6)	43.3	(9.6)	.059 §
Secondary gain (yes): n (%) Missing item values: n (%)	33 3[a]	(40.7)	27 2[a]	(41.5)	6 1[a]	(50.0)	.586
Satisfaction with accessibility of health care services: mean (SD)	3.7	(.7)	3.7	(.7)	3.9	(.7)	.341

* significant difference p<.05, ** significant difference p<.01, § difference p<.1
a Excluded pairwise from further analysis

Table 3 depicts the results of the bivariate analyses as a sub-step of the study analyses and the final results of the procedure using the multivariate logistic regression analyses, performed with non-response as the dependent variable

As shown in table 3, only the "gender" and "secondary gain" variables were associated with non-response measured with the SCL-90-R. Patients that at baseline reported hopes to obtain external benefits by seeking treatment, appear to have a lower chance of showing non-response to treatment as measured at 1-year follow-up when looking at the final results of the multivariate regression analyses (p=.054). This while males tend to have a higher chance of showing non-response (p=.074). No interaction effects were found. However, the fit statistics for this model are low: Mc Fadden's pseudo R-square equals 0.07 and

Table 2. Clinical characteristics of the study sample of completers and patients lost to follow-up (original data)

	Total Sample (n=81)		Study completers (n=68)		Patients lost to follow-up (n=13)		P-values between group differences: Study completers vs. Patients lost to follow-up
Primary diagnosis: n (%)							
Panic disorder	31	(38.3)	27	(39.7)	4	(30.8)	.54
Social phobia	16	(19.8)	11	(16.2)	5	(38.5)	.064 §
OCD	7	(8.6)	6	(8.8)	1	(7.7)	.894
GAD	6	(7.4)	5	(7.4)	1	(7.7)	.966
PTSD	16	(19.8)	14	(20.6)	2	(15.5)	.666
Specific phobia	3	(3.7)	3	(4.4)	0	(0.0)	.999
Hypochondria	2	(2.5)	2	(2.9)	0	(0.0)	.999
Comorbid axe I Diagnosis (yes): n (%)	30	(37)	27	(39.7)	3	(23.1)	.255
Total number of axe I diagnoses: mean (SD)	1.41	(.6)	1.4	(.6)	1.2	(.4)	.150
Comorbid anxiety disorder (yes): n (%)	9	(11.1)	9	(13.2)	0	(0.0)	.164
Comorbid mood disorder (yes): n (%)	17	(21.0)	14	(20.6)	3	(23.1)	.840
PDQ-4 score; personality disorder probable (yes): n (%)	29	(35.8)	27	(43.5)	2	(20.0)[b]	.159
Missing item values: n	9[a]		6[a]		3[a]		
SCL-90-R total-score: mean(SD)	192.8	60.8	195.7	(63.1)	177.9	(46.1)	.336
Treatment drop-out: n (%)	23	(28.4)	19	(27.9)	4	(30.8)	.836

§ difference p<.1
a Excluded pairwise from further analysis

ROC = 0.66, which indicates that the discrimination between responders and non-responders based on this model is rather poor.

Table 4 presents the results of the bivariate and multivariate analyses with persistent functional impairments measured with the SDS as the dependent variable.

Table 3. Predictors of non-response on the SCL-90-R (change score less than 30 points), with estimated values based on the imputed dataset (n=81).

Determinants	Bivariate			Multivariate		
	OR	95% CI	p	OR	95% CI	p
Age in years	1.03	0.99-1.07	.211	X		
Gender (male vs. female)	2.18	0.78-6.12	.139	2.80	0.91-8.66	.073
Background (foreign vs. native)	2.12	0.53-8.49	.289	X		
Having completed only primary school or less (yes vs. no)	1.22	0.28-5.38	.789	X		
Employment status (unemployed vs. employed)	0.59	0.23-1.58	.298	X		
Net monthly income in Euros	1.00	0.99-1.001	.783	X		
NML2 preparedness score	0.96	0.90-1.02	.215	X		
Secondary gain (yes/no)	0.42	0.15-1.18	.100	0.33	0.11-1.02	.054
Satisfaction with accessibility health care services: (less than satisfied vs. satisfied or very satisfied)	1.57	0.59-4.18	.365	X		
Comorbid anxiety disorder present (yes/no)	0.73	0.17-3.18	.671	X		
Comorbid mood disorder present (yes/no)	0.57	0.16-1.97	.370	X		
PDQ-4 score; personality disorder probable (yes/no)	0.67	0.24-1.85	.434	X		

As shown in table 4, the variables of "satisfaction with accessibility of health services", "gender" and "presence of comorbid anxiety disorder" were associated with persistent functional impairments. The results show that when comparing patients that express being less than content with the accessibility of care, with patients that express being content or even more satisfied with the accessibility, the first group has a higher chance of showing persisting functional impairments at 1-year follow-up. A result that is highly significant (p=.008). Also, males tend to have a higher chance of persisting functional impairments as measured at 1-year follow-up (p=.087). Surprisingly, compared to patients without such comorbid condition, patients who were at baseline found to suffer from another comorbid anxiety disorder appear to have a lower chance of persisting functional impairments (p=.079). Again, no interaction effects were found. The fit statistics for this model, predicting functional impairment based on these three predictor variables, are quite good: Mc Fadden's pseudo R-square equals 0.30 and ROC = 0.82, indicating an excellent

Table 4. Predictors of persistent functional impairments (a total score of 6 or higher on the Sheehan Disability Scale at 1-year follow-up), with estimated values based on the imputed dataset (n=81).

Determinants	Bivariate			Multivariate		
	OR	95% CI	p	OR	95% CI	p
Age in years	1.05	0.99-1.11	.067	X		
Gender (male vs. female)	2.68	0.84-8.53	.096	3.84	0.82-17.89	.087
Background (foreign vs. native)	0.82	0.17-3.94	.800	X		
Having completed only primary school or less (yes vs. no)	4.06	0.45-36.62	.212	X		
Employment status (unemployed vs. employed)	0.81	0.28-2.34	.699	X		
Net monthly income in Euros	1.00	0.99-1.001	.463	X		
NML2 preparedness score	0.97	0.91-1.04	.436	X		
Secondary gain (yes/no)	1.02	0.36-2.87	.972	X		
Satisfaction with accessibility of health care services: (less than satisfied vs. satisfied or very satisfied)	18.29	2.49-134.56	.004	27.84	2.38-325.46	.008
Comorbid anxiety disorder present (yes/no)	0.26	0.05-1.33	.105	0.11	0.01-1.29	.079
Comorbid mood disorder present (yes/no)	1.77	0.47-7.21	.423	X		
PDQ-4 score; personality disorder probable (yes/no)	1.33	0.46-3.89	.600	X		

degree of discrimination between patients with and without persistent functional impairments as measured at the 1-year follow-up.

To further study the results with respect to the predictive value of "gender"; "secondary gain" and "presence of a comorbid anxiety disorder", we compared baseline scores on the SCL-90-R of the predictor variables. It was found that males scored significantly lower on the SCL-90-R at baseline than females (mean total score= 173.56 versus mean total score= 203.60; t=-2.52, df=78.88, p=.014). Also, patients who at baseline reported their hope of obtaining external benefits by seeking treatment scored significantly higher on the

SCL-90-R at baseline, compared to the patients who did not (mean=211.62 vs. mean=179.38; z=-2.39, p=.017; calculations based on the imputed data). Baseline severity scores were found to be significantly related to symptom severity at the 1-year follow-up (r= .479, p<.001). Differences in baseline symptom severity thus might be a relevant confounding factor when studying the relationship between gender, secondary gain and treatment (non-)response.

Additional analyses of the results on functional impairment did not reveal differences on the SDS on the predictor variables of "gender", "comorbid anxiety disorder" and "accessibility of health care services", suggesting no confounding due to baseline differences.

5.4. Discussion

This practice-based study examined the predictive value of variables that are known to be able to influence treatment prognosis in anxiety disorder patients. These variables were examined in concert in a sample of 81 patients treated in a specialized mental health care setting who were judged to have been adequately treated according to evidence-based guidelines. We tried to develop a prediction model that allowed the identification of patients who run the risk of showing treatment non-response or who will continue to experience functional impairments when being provided guideline concordant care.

Of the demographic variables considered (age, gender, foreign background, educational level, employment status and income) only gender was identified as a potentially relevant predictor variable for both treatment non-response and persistent functional impairments. Males had a higher chance of showing treatment non-response and also a higher chance of having persistent functional impairments at the 1-year follow-up. However, males were found to have lower baseline symptom severity scores than females which might explain the results pertaining to treatment non-response. The data suggest that gender as a predictor of persistent functional impairments may have something to do with a subgroup of males quitting treatment prematurely. Of the patient characteristics, hope of secondary gain and the presence of a comorbid anxiety disorder were identified as being potentially relevant to treatment prognosis.

Contrary to what was expected from prior research [22], patients who reported a hope of gaining external benefits actually had a lower chance of showing treatment non-response. These patients were found to suffer from more severe general psychopathology at the baseline. It may be that the

reported motives for secondary gain might reflect a genuine need for help in managing life. This suggests that as long as additional support is available in addition to the regular evidence-based care for anxiety disorders, for example the availability of a community psychiatric nurse, greater treatment effects can be achieved in these patients. Patients who suffered from a comorbid anxiety disorder at baseline were also found to have a lower likelihood of persistent functional impairments. On the other hand, patients who were less than satisfied with the accessibility of health care services had a substantially greater risk of persistent functional impairments. Actually, this was the only study result that was significant when maintaining the orthodox significance level of 5 percent and therefore probably the most relevant result.

There are some limitations to the results of the current study. One of the most important issues is the relatively small sample size used in this study. In addition, because of the small sample size and the explorative nature of our study we maintained a liberal significance level of .10 for the selection of predictors. This makes replication of our study necessary. The small sample size may explain why the results for some of the predictors of treatment prognosis identified as relevant in other studies failed to reach significance in the current study. While this may be true, the size of the estimated Odds Ratio's in our study do suggest however that the influence of these variables is probably not very strong. This is likely to be especially true in a situation where patients get to choose among recommended evidence-based treatment options and can also receive multiple evidence-based treatments at the same time, as is the case in everyday clinical practice, as opposed to the more controlled circumstances of most predictor studies. Another limitation of the current study might be the fact that the treatment results were measured only at the 1-year follow-up. Some of the variables studied may have predictive value when studied over a shorter time period. The one-year time period for measuring treatment results was chosen in this prediction study on guideline concordant care because one year is the minimum length of time for the main recommended treatment steps to be put in effect for most anxiety disorders, in order to determine if there has been a sufficient treatment response.

There are several strengths to the present study. The patients included in the study sample are representative of "real world" mental health care. There were almost no exclusion criteria. To our knowledge the study presented here is also the first to look at the conglomerate of possible predictors of treatment response that have been identified as relevant to predicting treatment prognosis [2, 3] at the same time. This was done in a setting where patients were able

to choose among several available evidence-based treatment options and were also able to receive a combination of treatments when the clinician adhered to treatment guidelines for anxiety disorders.

From the results of the present study it can be concluded that it is hard to predict which anxiety disorder patients will or will not profit from guideline-adherent treatment in terms of demonstrating adequate treatment response. Unfortunately, this means that for the time being selecting an effective cure for the individual patient will for the most part remain a process of trial and error.

However, we may also conclude that with the knowledge currently available no one suffering from an anxiety disorder as a primary diagnosis should be prevented from being offered some form of evidence-based care according to the available evidence-based treatment guidelines, if one adapts to gender and removes barriers in attending treatment.

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CHAPTER 6

General discussion

6.1. Introduction

As was set out in the introduction to this thesis, there is still much to be done to improve the quality of health care. Evidence-based practices are being adopted in clinical practice at a rate that is far too slow. This is also true of the care provided to patients with anxiety disorders, a prevalent and disabling group of mental disorders. Delays in implementing these practices come at the expense of potential health gains that could be achieved with the proper implementation of available evidence-based treatment interventions and at the expense of the well-being of this group of patients. The effective use of these types of interventions is commonly expected to improve treatment outcomes.

The development and introduction of clinical practice guidelines has been a significant reaction to the slow speed at which evidence-based practices have been adopted. In the Netherlands, a substantial investment has been made to develop such guidelines for mental health care. The first guidelines for mental health care, published in 2003, dealt with the treatment of anxiety disorders. The aim is that by publishing guidelines such as these, knowledge about the scientific evidence supporting specific practices will spread more easily among healthcare practitioners, leading to quicker adoption of evidence-based treatments in clinical practice. Furthermore, the expectation is that the successful implementation of such guidelines will reduce unwanted variations in health care practices and improve the quality of care.

However, at the time the initial guidelines were published, little was known about how to achieve these aims. Actually, it was not even known whether the implementation of the available Dutch multidisciplinary guidelines for mental health care was feasible at all. Convincing evidence that adhering to such guidelines, and that the successful implementation of these guidelines in mental health care practice would indeed improve treatment results was scarce, and it was completely absent in the field of provision of care for anxiety disorder patients. Although the general expectation was that the successful

implementation of guidelines for anxiety disorders would lead to better treatment outcomes, not every patient was expected to profit sufficiently from treatment tailored to such guidelines. For clinical practice it would be very valuable to be able to identify reliable risk factors for non-response to treatment, even when treatment is delivered according to the multidisciplinary guidelines. An important question therefore was whether it is possible to predict which patients would not benefit from treatment adhering to the anxiety disorder guideline recommendations.

Our research project focuses on improving mental health care for anxiety disorder patients by implementing clinical practice guidelines. Therefore, it aimed to: 1) evaluate the feasibility of implementing anxiety disorder guidelines and look at possible implementation strategies that can be helpful in doing so; 2) evaluate the added value to treatment outcome of adhering to such guidelines; 3) evaluate the effectiveness of the implementation of guidelines in specialized mental health care; and 4) identify factors that predict non-response and persistent disability when treatment is guideline-adherent.

In this chapter the results of our efforts to realize these four aims will be summarized below, point by point. The summary starts with a discussion of the limitations followed by an outline of the strengths of the evidence regarding the different conclusions drawn from the studies that were performed to achieve these aims. Subsequently, recommendations for future research will be given. This chapter will close by summarizing the general conclusions of the research project and by highlighting the implications for clinical practice.

6.2. Discussion of key findings with respect to the feasibility of implementing clinical practice guidelines for anxiety disorders

Results from our case study (Chapter 2) regarding the implementation of the Dutch multidisciplinary guideline for anxiety disorders.

The Dutch multidisciplinary guidelines for anxiety disorders were systematically implemented in a specialized treatment unit for anxiety disorders in the Almelo community mental health care centre. Following the suggestions of Grol and Wensing [1], a stepwise and tailor-made approach to guideline implementation was used that comprised several multifaceted implementation strategies. As a first step quality of care was determined at baseline and goals for improvement were formulated. Also, a questionnaire to measure factors that

could hamper or facilitate implementation of the guidelines was developed and administered. The responses given by the members of the treatment unit for anxiety disorders on this questionnaire were used to direct the selection of interventions used to accommodate the implementation process. The main interventions that were used in the subsequent implementation steps included the following: redesign of the care process and standardization of the diagnostic process; development and distribution of instruction materials; educational meetings and training of professionals in the skills needed to perform treatment as suggested in the guidelines; and on-going monitoring of guideline adherence with regular provision of feedback on performance. After studying the medical records of 150 patients with an anxiety disorder or hypochondriasis who had been previously treated, and 181 patients who were treated after the start of the implementation activities, a significant increase was found in the number of patients who had been provided recommended forms of psychotherapeutic treatment over time. The percentage of guideline adherence with respect to the provision of recommended psychotherapeutic treatments increased by 43% to 54%, depending on the specific treatment method studied. Adherence to the recommended pharmacotherapeutic treatment steps remained stable during the process of implementation. However, adherence to the pharmacotherapeutic treatment steps was considered to be quite adequate even before the implementation was begun, and thus less relevant to change. Moreover, the number of patients indicated for these treatment steps appeared to be rather small. The increase in adherence to certain key recommendations of the guidelines could not be attributed to differences in patient characteristics in the two patient samples that were compared. Taken together, these findings suggest that it is possible to achieve meaningful changes in healthcare provider behaviour with regard to guideline adherence, and that with goal-directed and systematic efforts it is indeed feasible to implement clinical practice guidelines for anxiety disorders in a mental health care setting.

Limitations

Although the results of our case study look promising with regard to the feasibility of implementing anxiety disorder guidelines, it must be noted that significant increases in guideline adherence were only found for aspects of care that were explicitly targeted for change. Overall practice of care in the treatment unit studied still had room for improvement with respect to the adequate provision of psychotherapeutic and especially pharmacotherapeutic treatment, despite the systematic efforts aimed at implementation of the

guidelines. Whether it is possible to implement the guidelines almost perfectly and change care so that nearly 100% of the guideline recommendations are properly applied in clinical practice has not been definitively proven. One could argue that this limits our conclusion regarding the feasibility of implementing the guidelines. However the necessity for further improvement of certain aspects of care should have been used as input for another plan-do-check-act cycle to further increase guideline adherence. The implementation of guidelines must be viewed as a continuous process. The research group is quite confident that further improvements in adherence to the guideline recommendations could have been achieved with proper efforts and more time.

One limitation of the design of our case study is its dependence on patient medical files to assess guideline adherence. It leaves open the possibility that the improvements in adherence rates that were found over time do not reflect actual changes in health care provider behaviour, but only changes in record keeping. In addition, the set of process indicators, although carefully selected, constitute only rough measures of actual health care performance. However, this method of data collection and determining adherence to recommended treatment steps was chosen because it was relatively easy to carry out and did not require a special effort by the therapists involved in the study. We tried to increase the chances that the changes obtained would actually show the effect of the implementation strategies used instead of only an increased awareness of therapists being under scientific scrutiny. For instance, had we used audio or video tapes of treatment sessions to assess performance, the content of these sessions could possibly have been compromised by the fact that the professional would exhibit behaviour thought to be more 'desirable' because he/she felt under explicit scientific scrutiny. Additionally, we wanted to make sure that our implementation approach could be reproduced by other mental health care centres that want to implement the multidisciplinary anxiety disorder guidelines. We expected that if implementation necessitated recording treatment sessions to monitor guideline adherence, it could deter others from using this approach.

A second methodological limitation is the use of a before-and-after design, and the absence of a proper control condition and randomisation procedure. Thus it is impossible to be certain that the increase in adherence to certain guideline recommendations reported in the case study actually resulted from our implementation efforts and the effectiveness of our implementation approach. The established changes in healthcare provider behaviour may reflect the passing of time and changing opinions. With regard to this reported shortcoming, it is important to note that the case study was designed primarily to assess the feasi-

bility of implementing the guidelines, and not set up to assess the actual effectiveness of our implementation approach. However, as described in Chapter 2, studies by Bauer [4] and Weinmann and colleagues [5] show that without active efforts to ensure the implementation of a guideline, they adherence will only be marginal. Furthermore, recent research suggests that multidisciplinary guidelines in the Netherlands are actually rarely used by healthcare practitioners, despite their dissemination [6]. These findings suggest that the adherence rates found in our study have been influenced by our implementation activities.

Questions could be raised about the generalizability of the study results. The guidelines were implemented in one treatment unit only. The use of the specially developed questionnaire to measure factors that could hamper or facilitate implementation of the guidelines showed that members of this unit had attitudes towards the guidelines that were quite positive, even before the start of the implementation activities, and they expressed strong intentions to begin using the guidelines. This could have meant that the implementation of the guidelines was easier in this setting than it would be in situations where this was not the case. In such situations it is to be expected that more time and focussed interventions would be necessary to promote a positive attitude toward the guidelines, as an essential prerequisite for successful implementation. However, the results of the 'Breakthrough project for anxiety disorders' [2], which took place in the Netherlands between December 2006 and May 2008, can be seen as additional evidence of the feasibility of implementing recommended care according to anxiety disorder guidelines in everyday clinical treatment settings. In this project, 13 multidisciplinary teams from primary and secondary care collaborated with a panel of expert professionals to improve quality of care for patients with an anxiety disorder. This was done by adopting a stepped-care approach incorporating several selected recommendations in the multidisciplinary guidelines for anxiety disorders [2]. The results of this project suggest that important improvements in healthcare practice can be achieved, and that healthcare providers can be assisted in further embracing evidence-based practices and practice guidelines for anxiety disorders [2]. In addition, the breakthrough project suggests that improvement generally requires a deliberate and quite intense effort that should be maintained over a longer period of time.

Strengths

Our case study was the first systematic evaluation of the feasibility of implementing evidence-based practice guidelines for anxiety disorders worldwide. The study was carried out with more scientific rigor than the anxiety break-

through project that was also performed in the Netherlands [2]. We evaluated guideline adherence by performing a thorough review of medical records and by using a carefully developed set of process indicators, which reflected recommended treatment interventions based on high-quality scientific evidence. The final selection of recommended treatment options, on which the final set of process indicators used in this study was based, reflected parameters in need of change and relevant to quality of care, according to an expert group of professionals all of whom were members of the Dutch Knowledge Centre for Anxiety and Depressive Disorders (Nederlands Kenniscentrum Angst en Depressie).

To judge whether guidelines were properly adhered to, additional assessments were performed to establish whether the evidence-based interventions in the recommended treatment steps were carried out in accordance with state-of-the-art standards (for psychotherapeutic treatments this included: provision of a clear treatment rationale, appropriate homework assignments, and provision of treatment for the minimal recommended number of treatment sessions for the treatment to be effective; for pharmacological treatment it included the prescription of the correct category and type of drug, prescription of the correct dosage and the correct minimum duration of the medication before evaluation). The corresponding main process indicator was scored positively only when all of these additional performance assessments were fulfilled according to guideline recommendations. Furthermore, the study was carried out in a routine mental health care setting, using two representative and comparable patient samples to assess changes in guideline adherence over time. Actually, almost no formal exclusion criteria were used for patient inclusion. Any patient with a primary diagnosis of anxiety disorder or hypochondriasis could be included in the study. This ensured that the feasibility of implementing practice guidelines for anxiety disorders could be evaluated in the widest possible range of patients, including patients with a foreign background. This factor does not appear to have hampered proper guideline adherence.

The method of implementation described in our case study can be used in other situations. The implementation aids we developed, such as the desk-top guides and patient information materials, can be easily distributed and do not need to be developed all over again. Furthermore, in daily practice small samples of about ten medical records can be used as input for the plan-do-check-act cycle to monitor progress in implementing the guidelines. The set of process indicators to measure guideline adherence is available, and only needs slight changes given the recent revision of the Dutch anxiety disorder

guidelines. Both the questionnaire and the set of process indicators have been published in Dutch [7, 8] and international journals [9] and are thereby readily available to others. By performing our case study, we hope to have delivered an implementation methodology and a set of concrete implementation tools that makes replication of our study as easy as possible.

6.3. Discussion of key findings with respect to the added value of adhering to practice guidelines for anxiety disorders

Results from the cohort study (Chapter 3) that focused on the association between guideline adherence and treatment results

Using data collected on the treatment results for 181 patients who were included after implementation activities were begun in the Almelo community mental health centre, referred to in paragraph 6.2, we found that patients whose treatment adhered to the guidelines showed significantly greater symptom reduction as measured with the SCL-90-R, compared to those patients whose treatment did not adhere to the guidelines. In addition, the first group of patients had significantly fewer treatment contacts. Patients who received guideline-adherent treatment also reported a greater degree of satisfaction with their treatment. Although a significant improvement in functioning, in patient-reported quality of life and in general health was attained in the total sample of patients, the influence of guideline-adherent care concerning these aspects of outcome was not significant. Taken together, the results of our study suggest that guideline adherence does matter, not only with regard to symptom reduction, but also in terms of patient satisfaction with treatment and possibly with regard to efficiency as well.

Limitations

A limitation of the study is that the impact of guideline adherence was studied only in the group of patients included after implementation of the guidelines was begun in the centre, acting as a closed cohort. Although care was taken to rule out the possible influence of confounding factors as much as possible, causal inferences should be made with caution. Because of the chosen research design, it is not certain that there is not an unmeasured background variable that explains the fact that, in the same group of patients, the healthcare providers involved deviated from the guideline recommendations and the poorer patient response to treatment. In the study, patients whose treatment

did not adhere to the guidelines were found to have higher levels of general psychopathology, as reflected by higher baseline SCL-90-R total scores, more comorbid depressive symptoms, and a more frequent incidence of personality pathology. These patients also had a higher number of treatment contacts. In the statistical analysis of all of these variables, only the number of treatment sessions was found to relevantly confound the relationship between guideline adherence and treatment outcome, which was measured using a residual gain score. The number of treatment contacts was therefore added as an additional independent variable in our regression analysis to correct for this confounding factor, to obtain the final results, which were still positive, regarding achieved symptom reduction in the guideline-adherent patient group.

Strengths

Concerning the findings on the feasibility of implementing the anxiety disorder guidelines, the use of medical files and the use of the set of specially developed process indicators to determine adherence to key recommendations of the guidelines were brought up as a possible limitation of the study as described in paragraph 6.2. This means of measurement might provide only a superficial impression of the actual quality of care. With the above-mentioned cohort study it was possible to show that this type of measurement has clinical relevance, since a significant relationship could be established between the variable guideline adherence, based on the scores on the set of process indicators and the final treatment results obtained. Almost 12% of the variance in the outcome measure of patients receiving treatment was explained by the variable guideline adherence. This suggests that the method used for determining proper guideline adherence actually has predictive value for treatment outcome and bares relevance as a measure of quality of care.

Since data was collected in a routine mental health care setting, with patients representative of specialized mental health care in the Netherlands, this study permitted the assessment of the overall applicability of the anxiety disorder guidelines in everyday clinical practice. Some situations routinely encountered in clinical practice were considered proper justifications for a healthcare professional to decide not to apply a particular guideline recommendation: revision of the primary anxiety disorder diagnosis; a patient who refused recommended care or dropped out of treatment at a very early stage of treatment, making it impossible for the professional to provide adequate care; greatly interfering psychosocial problems; suicidality or addiction problems that had to take treatment priority. With pharmacotherapeutic treatment, additional legitimate

reasons for justifying that a particular recommended treatment step not be taken included: severe side effects, or a somatic contra-indication to pharmacotherapeutic treatment. In the sample used in the cohort study, it was established that in only 13% of the cases *none* of the guideline recommendations could be applied, due to the presence of one or more of the above-mentioned reasons. This suggests that the Dutch multidisciplinary guidelines for anxiety disorders are actually very applicable in everyday outpatient clinical practice.

6.4. Discussion of key findings with respect to the comparison in effectiveness of implementing practice guidelines

Results from the study described in Chapter 4, which compared adherence rates and treatment outcomes between two treatment centres for anxiety disorders during a two-year follow-up period.

In the study presented in Chapter 4 guideline adherence rates and treatment outcomes between two treatment centres for anxiety disorders were compared. One of these was the Almelo community mental health care centre of in which the guidelines had been systematically implemented. The other was a specialized treatment centre for anxiety disorders located in Amsterdam in which only passive dissemination of these guidelines took place. This means that in the Amsterdam centre the anxiety disorder guidelines were distributed among the healthcare providers as printed booklets, which made it easier for them to become familiar with the content of the guidelines. The Amsterdam treatment centre participated in the NESDA study, a naturalistic cohort study on the long-term course and consequences of depressive and anxiety disorders [10]. Data about treatment outcome at a 1-year and 2-year follow-up was available for patients in this centre with a primary diagnosis of panic disorder with or without agoraphobia, social phobia and generalized anxiety disorder. By confining the sample of patients of the cohort study that was performed in Almelo to study the added value of adhering to practice guidelines (see paragraph 6.3) to patients with one of these three disorders (intervention condition), it became possible to expand the original single cohort study and add a passive control group of patients treated in a setting in which only passive dissemination of the guidelines took place (control condition). Guideline adherence rates, as measured during the first year of treatment, were found to be significantly higher in the setting in which the guidelines were actively implemented. Patients in this intervention condition also showed superior treatment gains

on anxiety and avoidance symptoms at the 1-year follow-up, with small to medium between-group effect sizes on the anxiety disorder-specific outcome measures. At the 2-year follow-up, the difference in treatment gain from baseline to follow-up on anxiety symptoms between the two conditions was no longer significantly different. However the decrease in avoidance behaviour as measured from baseline to the 2-year follow-up still remained larger in the intervention condition. It was also established that in the control condition a significantly larger percentage of patients continued treatment after the first year of treatment. As a result, patients in the control condition seem to have partially caught up with the patients with respect to long-term treatment gain in terms of reducing anxiety symptoms. We are also able to demonstrate in both conditions that adherent treatments yielded superior outcomes than non-adherent treatments. It is therefore plausible that the difference in outcome found between the two conditions could indeed be attributed to the difference in adherence. Overall the data suggest that the active and systematic implementation of guidelines leads to greater treatment gains with respect to anxiety symptomatology, especially in the short term. Moreover, treatments which were adherent to the guidelines were of shorter duration, indicating that implementation of guidelines might improve the efficiency of care from a long-term perspective.

Limitations

There are some limitations to the study that must be addressed. First, because of the non-randomized nature of this 'double cohort' study design, we have to take into account the possibility that our findings might be influenced by confounders and be alert to other possible explanations for the established results. Both treatment centres appear to have been quite similar with regard to the number, the mean age, and the type of health care professionals on staff. Where differences existed in the composition of professional staff in the centres at the start of our study, one would expect that these would actually favour the results obtained in the control condition. For instance, the staff in the control condition centre, especially the psychologists, had more years of experience in working with patients suffering from an anxiety disorder. Furthermore, the staff in the control condition centre also expressed that they experienced a greater degree of control over their work processes. They rated their knowledge of the guidelines as higher and said that they experienced more normative social pressure to adhere to the guidelines before the start of the implementation/dissemination of the guidelines.

Both cohorts of patients appeared to be quite similar in composition except that the patients in the control condition were more highly educated and reported less severe anxiety symptoms and avoidance behaviour at baseline. The difference in education was found not to confound the relationship between the treatment condition and treatment outcome, operationalized as raw change in symptom severity from baseline to follow-up on the different outcome measurements. This might give the impression that patients with more severe baseline anxiety and avoidance symptoms could be the ones to have the greatest treatment gains. If this was correct, the baseline difference between the two conditions would be responsible for the superior treatment effect of the intervention compared to the control condition. The relationship between the severity of baseline symptoms and treatment gain, however, is equivocal: there is a great deal of literature showing that more severely anxious patients might actually profit less from treatment. See for example the recent article by Taylor et al. that summarizes several studies providing evidence for this case [11]. Remember also that in our single-cohort study (see paragraph 6.3), patients who were labelled as non-adherent cases were found to suffer from higher levels of general psychopathology and showed less treatment gain compared to patients who were labelled as having received guideline adherent treatment. Because of these findings, it can be argued that there is a lesser chance of finding superior results in the intervention condition, in terms of greater guideline adherence and treatment outcomes, because more severe anxiety symptomatology was reported by the patients at baseline in this condition. Due to the observational nature of our study, we wanted to be as transparent as possible about differences between the treatment settings and the patients treated there. Therefore we primarily reported the raw change scores and not 'residual gain scores' that can be calculated by using a patient's mean change scores over time, after correction for the baseline severity scores. The use of residual change scores is appropriate when it is safe to assume that a patient actually has the same chance of being assigned to either an experimental or control condition, and when baseline differences in patients between the two conditions can only be the result of chance. However, as a check we performed additional analyses using residual gain scores, correcting for the baseline differences between the two research conditions. These additional analyses for the most part corroborated the analyses with raw change scores and we therefore chose to report the uncorrected outcomes. Our results are also in line with the findings from the study by Verbeke et al., which investi-

gated the influence of making baseline corrections when using longitudinal data and suggested that this makes no difference [12].

A direct relationship was also found between guideline adherence and treatment outcome as measured at the patient level, yielding significant relationships on all continuous outcome measures. This to a large extent rules out the possibility of an ecological inference fallacy and when studied more directly shows the relevance of adhering to the treatment guidelines. Possible alternative explanations for our findings concerning differences in treatment setting and patient characteristics are therefore considered less viable.

Strengths

Again, the use of two well-diagnosed cohorts of anxiety disorder patients, representative of secondary outpatient mental health care, can be seen as a methodological strength of our study. The patients we included are particularly representative of 'real life'' because we applied only one exclusion criterion (insufficient proficiency in the Dutch language), thereby enhancing the external validity of our study results.

Concerning the case study described in paragraph 6.2, it was stated that the lack of a control group rendered it impossible to draw any conclusions on the effectiveness of the implementation approach used in terms of changing healthcare provider behaviour. The changes in provider behaviour that were found in this study could for instance merely reflect the passing of time, and the fact that the recommended treatments described in the guidelines slowly became more common practice. However, since adherence rates in the double-cohort study were significantly higher in the intervention condition than in the control condition and because of the fact that adherence was measured during the same period of time, this adds to the evidence that the change in healthcare provider behaviour could be the result of the systematic implementation of the guidelines in the intervention condition. This is even more likely if one considers the fact that the control condition had a somewhat more favourable starting position with respect to presence of certain factors that could promote proper guideline adherence by the involved healthcare providers (e.g. the healthcare providers in the control condition had more experience in treating anxiety disorders, were found to have more knowledge about the content of the guidelines, and experienced more social pressure to adhere to the guidelines before start of the implementation). Of course definitive proof of the effectiveness of the implementation approach can only be

derived from a randomized controlled trial measuring changes in guideline adherence and changes in treatment results over time.

6.5. Discussion of key findings on the identification of factors that predict non-response and persistent disability when treatment is guideline-adherent

Results from the prediction study (Chapter 5) with respect to factors that can predict treatment non-response and persistent disability, when treatment adheres to evidence-based practice guidelines for anxiety disorders

By confining the sample of the single cohort study referred to in paragraph 6.3 to the 81 patients whose treatment was found to adhere to the anxiety disorder guidelines, it was possible to look at possible predictors of treatment non-response and persistent functional impairments when treatment properly adheres to the guidelines. The predictive value of several variables that are known to be able to influence treatment prognosis was studied, in conjunction, using multivariate logistic regression analyses.

Of the demographic variables studied (such as age, gender, foreign background, educational level, employment status, income) only gender was identified as a potentially relevant predictor variable for treatment non-response as well as persistent functional impairments when it pertained to a rather liberal significance level of 10 percent. Male gender was found to be associated with a higher rate of treatment non-response and also a higher rate of persistent functional impairments at the 1-year follow-up. Of the other patient characteristics (such as motivation for treatment, motives for secondary gain, the presence of comorbid depressive disorder, the presence of comorbid anxiety disorder, probable comorbid personality pathology), only secondary gain and the presence of a comorbid anxiety disorder were identified as having potential relevance to treatment prognosis when pertaining to the liberal significance level of 10 percent. Contrary to expectation, patients who at baseline reported hopes for gaining external benefits actually had a lower likelihood of non-response to treatment. Patients who at baseline suffered from a comorbid anxiety disorder were found to have a lower likelihood of persistent functional impairment after treatment. In addition, patients who were less than satisfied with the accessibility of the health care services were found to have a substantially higher rate of persistent functional impairment.

The predictive value of the constructed model for treatment non-response that contained the selected predictor variables of gender and secondary gain was found to discriminate poorly between treatment non-responders and responders. Therefore, it must be concluded that it is not entirely possible to predict which patients will or will not profit from a treatment that is tailored according to anxiety disorder guideline recommendations.

The prediction model for persistent functional impairment that contained the selected predictor variables of gender, presence of a comorbid anxiety disorder and satisfaction with the accessibility of health services was found to discriminate excellently between patients with and without persistent functional impairment. In terms of reducing the rate of persistent functional impairment, it seems that the most attention should be directed to situations in which a patient reports experiencing barriers that hamper treatment attendance, or expresses dissatisfaction with the accessibility of health care services. Offering e-health interventions, or visiting the patient at home for treatment, may provide a solution to this problem.

Limitations

One of the most important limitations of our study is the relatively small sample size used. Because of the small sample size and the explorative nature of our study we kept to a rather high significance level of .10 for the selection of predictors that were considered to be relevant. As a result some of the study findings could be the result of chance alone. Replication of our study will be necessary in order to assess whether the findings are generalizable to other patient samples.

Another limitation of the current study might be the fact that the treatment results were measured only at the one-year follow-up. Some of the variables studied (such as treatment motivation for instance) may indeed have a predictive value when studying treatment outcomes in the shorter run, but fail to show such an effect here due to the longer time-frame of the current study. The one-year time period for measuring treatment results was chosen because we wanted to investigate predictors of treatment non-response and persistent functional impairment in patients receiving guideline-concordant care according to available treatment algorithms. For the main recommended treatment steps in most anxiety disorders to be put into effect a time period of at least one year is required in case there is an initial insufficient treatment response. A larger study sample might have permitted the exploration of differential effects of certain predictor variables for certain types or combinations of treatment,

for example when some patients received only a single recommended treatment step and others a combination of multiple treatments. With the limited number of patients in this study we were not able to investigate this effect.

Strengths
As stated before we included patients who are representative of those seen in day-to-day outpatient clinical practice in secondary mental health care in the Netherlands. There were almost no exclusion criteria. To our knowledge the study described above is the first to look at the conglomerate of possible predictors of treatment response that have been identified as relevant to predicting treatment prognosis. Patients included in the study were able to choose among several available evidence-based treatment options for anxiety disorders and were also able to receive a combination of treatments that adhered to treatment guidelines for anxiety disorders.

6.6. Recommendations for future research

6.6.1. Issues concerning the implementation of practice guidelines for anxiety disorders

Although knowledge about effective interventions and strategies when aiming to implement guidelines for mental healthcare is slowly accumulating in the Netherlands (see for instance the 2009 Dutch Trend report for Mental Healthcare [6]), many questions regarding the implementation of these practice guidelines remain unanswered. One very important question is which implementation interventions are most effective and under what circumstances. Our implementation approach used interventions aimed at the organizational level for the most part (e.g. redesign of the care process) and the level of the health care provider (e.g. training, continuous feedback on performance). Only one was explicitly focussed on the level of the individual patient (distribution of patient instruction materials that provided disorder-specific information and the different recommended treatment options they could choose from). The interventions used were carefully selected based on the results of a diagnostic phase, in which an effort was made to identify relevant context-specific factors that could hamper or promote guideline adherence in the setting in which the guidelines were implemented. Although the literature (see also paragraph 1.4) and our research show this to be a potentially useful approach, due to the enormous number and differing types of available imple-

mentation interventions [13], other choices could easily have been made with respect to the specific interventions and the combination of interventions that were used in the present study. Factors that concern the macro and societal level, such as changes in legislation and financing issues (for instance, changes in the list of psychological interventions that are eligible for insurance reimbursement, designated by the Dutch Healthcare Insurance Board (CVZ)) may influence the uptake of recommended evidence-based treatments and adherence to available practice guidelines to a great extent. Future research should focus more on identifying the interventions that are most effective, and under which specific conditions. This enables well-considered choices to be made in developing a specific guideline implementation approach for a given situation.

For this purpose one ideally would perform a large-scale, cluster randomized controlled trial involving multiple specialized mental health care treatment centres/units, in which interventions take place at the level of the treatment setting. Before randomization these centres/units should be stratified according to geographical region and size, and perhaps additionally according to factors such as current knowledge of the guidelines, attitude towards the guidelines, experienced behavioural control in ability to apply the guideline recommendations and experienced normative social pressure to adhere to the guidelines. Ideally, this research would include adherence measurements at the level of the healthcare provider and measurements for establishing treatment results at the patient level. Our recommendations would be that this research would encompass at least three phases: one to establish baseline levels of guideline adherence and treatment efficacy, an implementation phase to allow establishment of the short-term effectiveness of the implementation strategies used and a follow-up phase to establish long-term results. In contrast to our research, this type of research would permit causal inferences about the effectiveness of implementing guidelines for anxiety disorders to be made. Preferably this study would investigate different combinations of implementation interventions for similar baseline circumstances, and would also include a neutral control condition in which no active implementation of the guidelines takes place. This research would also encompass measures to determine the cost-effectiveness of the chosen implementation strategies. Our research has made it clear that the implementation of guidelines for clinical practice requires quite intensive efforts that should be maintained for longer periods of time; therefore it would be very valuable to know if implementation, and which implementation strategies, are cost-effective. Of course this type of research would require substantial investment. However, with our research providing

evidence for the potential value of implementing guidelines for the treatment of anxiety disorders and the expectation that the successful implementation of guidelines would probably make treatment more efficient, it is our opinion that this would be worthwhile scientifically and also to society at large.

6.6.2. Issues concerning the content of the anxiety disorder guidelines

The investigated anxiety disorder guidelines contain different treatment algorithms that summarize the available evidence-based treatment options for a given anxiety disorder. These treatment options are put in order as recommended treatment steps, based on the level of existing scientific evidence, long-term effectiveness, and considerations regarding the possible toxicity and risk of adverse side effects of the available medicines, and ultimately also reflect the consensus of the expert group responsible for devising the guidelines. In general the evidence for the effectiveness of the single treatment steps is quite strong. However, scientific evidence for the described sequence of steps is almost completely lacking. For instance, the algorithm described in the guideline for the treatment of Posttraumatic Stress Disorder (PTSD) advises switching from Eye-Movement-Desensitization-Reprocessing (EMDR) to cognitive behavioural therapy (CBT), or to pharmacotherapeutic treatment when there is an insufficient treatment response to EMDR. No studies have been published describing the effectiveness of CBT after EMDR. It is also unknown whether switching to pharmacotherapeutic treatment after non-response to EMDR as an evidence-based form of psychological treatment might not prove to be a more effective strategy. Regarding pharmacotherapeutic treatment for most conditions, the anxiety disorder guidelines recommend trying several antidepressants, and in most cases two different SSRIs, before switching to another group of medications. For many anxiety disorders more than three pharmacotherapeutic treatment steps are described before the binding advice is given to switch to psychological treatment, before trying another, different type of medication. Our data suggest that most patients reject trying another type of medication, after having received two or three different drugs without sufficient treatment response. In other instances the practitioner considered switching medication that was contraindicated because of possible side effects. These findings stress the need for investigating the effectiveness of switching medication, within and between similar groups of drugs, after nonresponse. Ideally the effectiveness of these different recommended treatment steps, after insufficient treatment response to an earlier recommended treatment step, would be investigated in a randomized controlled trial. However, expanding the cluster randomized trial

as described in paragraph 6.6a, so that treatment results are measured after provision of each of the different treatment steps, could provide some insight into which sequence of treatment steps could improve effectiveness after an insufficient treatment response to one or more of the recommended treatment steps. A research project such as this might well be described as very ambitious. However, it is not much more ambitious than some of the projects funded by the National Institute of Mental Health (NIMH) in the United States (see www.nimh.nih.gov/funding/clinical-trials-for-researchers/practical/index.shtml). Forty-one clinical sites were involved in the well-known STAR*D study (Sequenced Treatment Alternatives to Relieve Depression Study) for instance, in which medication algorithms were implemented to study treatment response to subsequent treatment steps in non-responsive patients who suffered from major depressive disorder. Initially more than 4000 depressive patients were included in this study, according to the NIMH website. Examples such as these suggest that projects such as the one we suggest are indeed feasible with sufficient funding. In the future we should be able to predict in advance the likelihood of patients having an adequate response to the various treatment steps, according to certain patient characteristics (for example, using genetic/endophenotype profiles).

6.7. General conclusions and implications for clinical practice

Although the publication of the guidelines for mental health care in the Netherlands initially sparked an interest in their implementation and received a big impetus from the national breakthrough projects [3], in more recent years this interest seems to have diminished somewhat within specialized mental health care. Many mental health institutions nowadays seem to be occupied with other recent challenges, such as the large-scale introduction of Routine Outcome Monitoring (ROM), the changing financial structure and the decreasing budget for mental health care. The more recent development of the introduction of clinical care pathways may prove an alternative means for increasing the uptake of the recommended guideline interventions.

The budget for research/innovation grants that could help effectuate such projects also seems to be diminished. At the same time, one could also expect that these exact same developments would fuel the need to start to implement guidelines for mental health care on a far larger scale, and provide input to the scientific study of such implementation projects.

In an era in which health care services are increasingly held fiscally accountable and efficiency of care is demanded, one would expect healthcare providers to embrace evidence-based practice guidelines more often because they provide for transparency in care. In paragraph 1.3 it was stated that the implementation of guidelines might be especially effective in the treatment of less complex psychiatric disorders, for which several potent evidence-based treatment options exist. It has been shown that the results of implementation studies for severe mental illnesses, such as schizophrenia, are not entirely positive [13]. The results of our study on implementing guidelines for anxiety disorders are in line with the results of several newer studies on implementing guidelines for major depressive disorders that report positive results [14, 15, 16, 17]. Taken together, this line of research suggests that the implementation of practice guidelines, especially for affective disorders in clinical practice, is possible and also worthwhile. We would advise guidelines for this group of disorders to be implemented on a far larger scale. An essential prerequisite for achieving such a large-scale implementation is that insurance companies allow sufficient treatment durations for these recommended treatment options to be put in effect, preferably in primary care so that the first recommended treatment steps can be provided according to the guidelines.

At this time the existing evidence suggests that a systematic, tailor-made approach to guideline implementation seems to offer the best likelihood of successful implementation. Selected implementation interventions should target specific barriers to implementation, or match certain factors that could promote guideline adherence in a given context. We found the recommended implementation steps suggested by Grol and Wensing [18] to be very helpful. Measuring healthcare provider performance and the regular provision of feedback seem to be critical components of this implementation approach, and an essential prerequisite to being able to adjust the implementation approach if necessary. As mentioned before, we developed several practical tools that can be helpful and can easily be borrowed from our study since they were made freely available through publications which should make it easier for others to implement the guidelines for the treatment of anxiety disorders [7, 8, 9].

For clinical practice it seems important to keep in mind that the implementation of practice guidelines for anxiety disorders and probably the implementation of guidelines in general require a deliberate approach and intensive effort that should be maintained for a substantial length of time. Maintenance of the established implementation results over the longer term might prove especially challenging. Health care organizations should try to integrate healthcare

provider performance measures and use process indicators in a regular feedback loop, in addition to measures of treatment outcome. In this way they will be better able to understand variations in treatment results while patient characteristics remain constant. Subsequently, they have the ability to intervene in a timely fashion if important deviations from the care recommended by the guidelines are detected. Proper adherence to the guidelines and possible challenges to doing so should also be a topic of regularly held team meetings. Newcomers to a treatment unit should be educated on the content and proper usage of the guidelines. It seems wise to standardize this type of training and to offer it on a regular basis to keep all health care providers well-informed.

Our research showed the guidelines to be highly applicable to most patients seen in clinical practice. In the study described in Chapter 3 only very few cases were identified where it was established that none of the guideline-recommended treatment options could be provided, after interpreting the justifications for deviating from guideline recommendations recorded in patient records by the healthcare providers involved. As we did not find predictors to identify patients who run a clear risk of treatment non-response, we may conclude that we should be reluctant to deny a patient treatment according to the guidelines beforehand. Even in patients with various types of comorbid conditions it was possible to deliver at least some of the recommended treatment steps. If necessary it may be better to augment treatment according to the guidelines with additional supportive interventions, rather than withholding treatment altogether. The help of a psychiatric nurse or referral to a crisis support service do not necessarily have to preclude treatment according to guidelines. Of course, in these instances, proper coordination of care might become more challenging.

In conclusion, the combined results of our research project suggest: 1) that the implementation of guidelines for the treatment of anxiety disorders in specialized mental health care is feasible; 2) that adhering to anxiety disorder guidelines is worthwhile; 3) that the implementation of anxiety disorder guidelines in this setting is effective (especially in the shorter run) and might possibly improve efficiency as well; and 4) that no patient should be denied treatment according to these guidelines as long as any barriers to treatment attendance are properly accounted for and care is taken to motivate patients who may be reluctant to switch therapies after a first treatment non-response especially in males, because no other factors were identified that could reliably predict treatment non-response or persisting functional impairments.

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CHAPTER 7

Summary

Scientific studies have demonstrated unequivocally that evidence-based healthcare interventions generally take far too long to be implemented in practice. Such delays could undermine the efficacy of treatment and thus place patients at a disadvantage. Moreover, potentially sub-optimal interventions will place an unnecessary strain on the healthcare budget and therefore on society as a whole. This problem could be solved by applying treatment guidelines, systematically developed standards that enable the results of scientific research to be translated into concrete recommendations for the treatment of specific disorders.

Since 2003, fifteen disorder-specific *multidisciplinary* guidelines have been published for the treatment of various psychiatric problems in the Netherlands. Indeed, the Dutch are front-runners in the development of guidelines for the treatment of mental health disorders. But these guidelines have not escaped criticism. For example, some critics question the value of adopting the medical model with DSM-IV diagnostic classifications as a starting point. Others argue that too much attention is paid to treatments that have proven efficacious in studies and not enough to practical experience: as the populations for efficacy studies are often subject to stringent selection criteria, the external validity of the results is limited.

The implementation of treatment guidelines is a challenge – which poses an underlying question. Will adherence to treatment guidelines actually pay off in general terms? This thesis focuses on the implementation of treatment guidelines for patients with anxiety disorders. The anxiety disorders in DSM-IV represent a phenomenally wide range of psychological conditions, all characterized by frequent, excessive and irrational feelings of anxiety and/or fear, which lead to suffering and disability. With an estimated 1.3 million sufferers, anxiety disorders are among the most prevalent psychiatric conditions in the Netherlands and a drain on the healthcare system. At the start of this PhD project, no research had been conducted on even the implementation of treatment guidelines for this patient population, let alone their effectiveness.

The thesis answers the following questions:

1) Is it feasible to implement the Dutch multidisciplinary guidelines for anxiety disorders in everyday clinical practice and, if so, what kind of implementation strategy can be helpful in doing so?
2) Would adherence to these guidelines deliver better results than non-adherence?
3) Would active and systematic implementation of multidisciplinary guidelines for anxiety disorders go hand in hand with better adherence to these guidelines and better healthcare results as opposed to passive dissemination?
4) Is it possible to predict which patients with an anxiety disorder will not respond to treatment in accordance with the guidelines and which patients will retain functional impairments?

Chapter 2 reports a case study that sought to determine whether the guidelines for treating anxiety disorders can be implemented in everyday mental healthcare practice and to identify the most effective ways of achieving this. The guidelines were systematically implemented in an ambulant team that treated anxiety disorders. This team, consisting of 16 professionals from different disciplines with varying degrees of seniority, formed part of a second-line treatment setting in Almelo. It applied Grol and Wensing's stepped implementation plan, which consisted of a diagnostic analysis at baseline (prior to implementation), the formulation of goals, and a specifically chosen combination of implementation strategies. The effects were monitored regularly, so that any necessary adjustments could be made along the way. The aim each time was to deliver a tailor-made programme based on the chosen implementation strategies and to evaluate the outcomes for the desired effect.

One important tool in the implementation was a set of process indicators, which was developed with input from members of the Dutch Knowledge Centre for Anxiety and Depressive Disorders (NEDKAD). The indicators took information from patient files in order to measure how far the main treatment steps in the guidelines had been applied properly. Another important tool was a newly compiled questionnaire for determining where the professionals stood with regard to the different constructs from the Theory of Planned Behaviour. The ultimate aim was to identify facilitative and impeding factors in the implementation. Five actions were eventually defined for the plan-do-check-act cycle: 1) Reorganize the care process so that the treatment plan is drawn up by the coordinator of the treatment team and not the intaker (who comes from an intake team); 2) Develop and disseminate instructions for care workers and patients about the recommended treatment in accordance with the guide-

lines; 3) Organize instruction sessions to discuss the content of the guidelines and the scope of the recommendations; 4) Train professionals in the skills required for proper application of the guidelines; 5) Measure regularly the extent to which the interventions are actually applied. The fifth action figured in the discussions on the treatment plan between individual care workers and the coordinator and in the feedback sessions with the entire treatment team. These sessions were held every few months to co-evaluate the progress of the project and to identify new areas of treatment.

A comparison of the results in the files of 150 patients who were treated in the anxiety disorder team prior to implementation with those of 181 patients who were treated in the same team after implementation pointed to significant improvements in adherence to the main recommendations in the guidelines. This demonstrates that it is possible to implement guidelines in a team that treats patients with anxiety disorders in a clinical setting. A stepped approach turned out to be useful here as it allowed specific obstacles to be addressed with tailor-made interventions.

Chapter 3 reports a study in which the treatment results were determined for anxiety disorder patients who were incorporated in the study after the guidelines had been implemented in Almelo. The aim was to ascertain whether adherence to the guidelines delivered better results. After one year the treatment results for 81 patients among whom the guidelines had been adhered to were compared with those of 58 patients among whom the guidelines had not been adhered to. The reduction in symptoms for the patients where the main guidelines had been adhered to was significantly greater than for the patients where they had not been adhered to. No significant difference in improvements to quality of life was found between the two groups. The group where the guidelines had been adhered to were, however, more satisfied with the treatment than the other group. The number of treatment contacts was also smaller in the group where the guidelines had been adhered to. The study concluded that the guidelines would be applicable to 87% of patients. Adherence to the guidelines can therefore lead to better results and more efficient healthcare. The study also showed that the recommendations in the guidelines can be applied across a broad spectrum.

Chapter 4 presents the results of a study which compared the cohort of patients from Almelo, who were included after the start of the implementation, with a cohort that was treated in a similar setting in Amsterdam, where the guide-

lines were disseminated only among the care workers that were employed there. The Amsterdam patients were part of the NESDA study (Netherlands Study on Depression and Anxiety). The aim of this comparative study was to ascertain whether systematic implementation of the guidelines – as described in Chapter 2 – would lead to better adherence and better treatment results than just passive dissemination. As the NESDA study was limited to patients with a primary diagnosis of panic disorder with or without agoraphobia, social phobia or generalized anxiety disorder, only patients with the same diagnosis were selected from the Almelo cohort for comparison. After a year of treatment it appeared that adherence to the main treatment recommendations was greater for patients in the treatment setting where the guidelines were systematically implemented (intervention condition). After a year, the responses to a questionnaire indicated a significantly stronger decline in anxiety symptoms for the patients in the intervention condition than for the patients in the control condition. After two years, however, this significant difference had disappeared; presumably because more patients in the control condition had been treated for a longer period of time. No difference was found between the two conditions for a decline in comorbid depressive disorders. These results suggest that if the guidelines were better applied, there would be opportunities for further improvements in the care outcomes. The conclusion is that systematic implementation of the anxiety treatment guidelines can improve the quality and possibly also the efficiency of healthcare.

Chapter 5 presents the results of a study on the possibility of predicting unfavourable outcomes for the group of 81 patients from Almelo where the guidelines were adhered to. The aim was to determine which patients with an anxiety disorder would not respond to treatment and which patients would retain functional impairments after one year of treatment in accordance with the guidelines. The predictive value of variables which had been shown in another study to be capable of influencing the treatment prognosis for patients was examined. Typical examples were age, gender, ethnic origin, educational background, working situation, income, motivation for treatment, motives for secondary gains, the existence of a comorbid depressive disorder, a comorbid anxiety disorder or a comorbid personality disorder, and the level of satisfaction with the accessibility of the care. The stepped selection procedure for developing a predictor of non-response to treatment delivered a model with only gender and motives for secondary gain as predictive variables. The likelihood of non-response to treatment after a year was slightly greater among

men and – surprisingly – smaller among patients with a secondary motive for seeking help. The predictive value of this model for non-response to treatment turned out to be very limited. The stepped selection procedure for developing a predictor of lasting functional impairments delivered a model with gender, a comorbid anxiety disorder, and satisfaction with the accessibility of the healthcare as predictive variables. The likelihood of lasting functional impairments after one year was greater among men and patients who were dissatisfied with the accessibility of the healthcare and smaller among patients with a comorbid anxiety disorder. The results indicate that this model, with its three predictive variables, is perfectly capable of distinguishing between patients with a greater or smaller likelihood of lasting functional impairments after one year. The conclusion for the time being is that, when we measure the outcomes on the basis of a response to treatment, it is not yet possible to predict which clients will not sufficiently benefit from treatment in accordance with the guidelines. This implies, at the same time, that with the current knowledge, there is little reason to deny such treatment to someone with an anxiety disorder as a primary diagnosis. To preclude long-term disability the care services should take on board the problems some people experience when trying to gain access to healthcare. Home visits or E-health interventions could offer a way forward in such cases.

Chapter 6 draws together and discusses the results of different subsidiary studies. It is difficult to draw definite and hard causal conclusions from these studies, since they were observational in nature. Follow-up research on the implementation of guidelines for the treatment of anxiety should take the form of a multi-centre, cluster-randomized, controlled experiment. It would also be useful to look into the added value of offering the successive recommended treatment steps in the guidelines. Ideally, better predictors of the success of the different treatment steps should be developed as more knowledge in this area would further improve healthcare efficiency.

Samenvatting: De toepasbaarheid en effectiviteit van de Nederlandse multidisciplinaire richtlijnen voor de behandeling van angststoornissen in de dagelijkse klinische praktijk

Introductie (hoofdstuk 1). Studies maken duidelijk dat bewezen effectieve interventies in de regel in een veel te laag tempo tot de zorgverleningspraktijk doordringen. Dit heeft nadelige consequenties voor patiënten doordat behandelresultaten kunnen tegenvallen. Als gevolg van het aanbod van mogelijk suboptimale interventies worden ook onnodig hoge ziektekosten gemaakt, hetgeen vooral nadelig is vanuit maatschappelijk perspectief. Een oplossing voor dit probleem vormt de ontwikkeling van behandelrichtlijnen. Binnen deze systematisch ontwikkelde standaarden wordt de vertaalslag gemaakt van resultaten uit wetenschappelijk onderzoek naar concrete aanbevelingen voor het handelen bij een bepaalde aandoening.

Sinds 2003 zijn inmiddels 15 van dergelijke stoornis specifieke *multidisciplinaire* richtlijnen voor de behandeling van diverse psychiatrische problemen gepubliceerd. Waar het gaat om de ontwikkeling van behandelrichtlijnen voor de Geestelijke gezondheidszorg (GGZ), behoort Nederland daarmee tot de koplopers. Deze richtlijnen zijn echter niet vrij van kritiek. Er worden verschillende tekortkomingen genoemd. Het medisch model als uitgangspunt met de DSM-IV classificaties als aangrijpingspunt voor de ontwikkeling van de richtlijnen worden door sommigen bijvoorbeeld niet als optimaal gezien. Een andere tekortkoming zou de eenzijdige nadruk zijn op behandelingen die bewezen effectief zijn, zonder recht te doen aan ervaringen vanuit de praktijk. Doordat effectiviteit vaak onderzocht wordt in *efficacy studies* met streng geselecteerde onderzoekspopulaties, zou de externe validiteit van de resultaten beperkt zijn.

De implementatie van behandelrichtlijnen vormt een uitdaging, waarbij een belangrijke vraag is of het nastreven er van in algemene zin ook daadwerkelijk de moeite waard is. In dit proefschrift ligt het focus op de implementatie van behandelrichtlijnen voor patiënten met een angststoornis. De groep van angststoornissen zoals onderscheiden binnen de DSM-IV omvat een fenomenologische diverse groep van psychische stoornissen, waarbij de patiënten die hier aan lijden als centraal kenmerk delen dat sprake is van frequent voorkomende,

overmatige en onredelijke angstgevoelens en/of buitensporige vrees, welke een duidelijk lijden en invalidatie met zich meebrengen. De schattingen zijn dat in Nederland ongeveer 1, 3 miljoen mensen aan een angststoornis lijden. Angststoornissen behoren daarmee tot de meest voorkomende psychiatrische stoornissen en gaan gepaard met een grote ziektelast. Ten tijde van de start van het onderzoeksproject, waarvan dit proefschrift verslag doet, bestond er geen onderzoek naar de mogelijkheid richtlijnen voor deze patiëntenpopulatie te implementeren laat staan naar de effectiviteit van een dergelijke implementatie.

Onderhavig proefschrift geeft antwoord op de volgende onderzoeksvragen:

1) Is het mogelijk de Nederlandse multidisciplinaire richtlijnen voor angststoornissen in de dagelijkse klinische praktijk te implementeren en welke aanpak is daarbij behulpzaam?
2) Levert het naleven van deze richtlijnen superieure uitkomsten op vergeleken met niet naleven van deze richtlijnen?
3) Gaat actieve en systematische implementatie van de multidisciplinaire richtlijnen voor angststoornissen gepaard met betere adherentie aan deze richtlijnen en met betere uitkomsten van zorg, vergeleken met passieve disseminatie?
4) Is het mogelijk te voorspellen welke patiënten met een angststoornis niet zullen reageren op een behandeling volgens de richtlijn en welke patiënten functionele beperkingen zullen blijven houden?

In *hoofdstuk 2* wordt verslag gedaan van een casestudie waarmee getracht is antwoord te vinden op de vraag of de richtlijnen voor angststoornissen in de alledaagse praktijk van de GGZ geïmplementeerd kunnen worden. Onderzocht werd wat effectieve manieren zijn om dit voor elkaar te krijgen. De richtlijnen werden systematisch geïmplementeerd binnen een ambulant behandelteam voor angststoornissen. Dit team vormde onderdeel van een tweedelijns behandelsetting in Almelo, bestaande uit 16 professionals van verschillende disciplines en niveau van senioriteit. Er werd gebruik gemaakt van de stapsgewijze aanpak voor implementatie beschreven door Grol en Wensing. Hierbij wordt na een diagnostische analyse van de uitgangssituatie voor implementatie en het formuleren van veranderdoelen, een gerichte keuze gemaakt werd voor een combinatie van implementatie-strategieën. Het effect werd met regelmaat gemonitord. Uitkomsten van het periodieke monitoren, konden aanleiding vormen om het implementatie plan bij te stellen.

Een belangrijk hulpmiddel bij de implementatie was een set van procesindicatoren. Deze indicatoren werden ontwikkeld door input van leden van het NEDerlands Kenniscentrum voor Angst en Depressie (NEDKAD). De indicatoren werden gebruikt om met de informatie uit de dossiers van patiënten een indruk te krijgen van de mate waarin de belangrijkste aanbevolen behandelstappen uit de richtlijnen goed toegepast werden. Een ander belangrijk hulpmiddel vormde een nieuw ontwikkelde vragenlijst voor het in kaart brengen van de positie van de professionals op de verschillende constructen uit de theorie van planmatig handelen, zodat belemmerende en bevorderende factoren voor de implementatie in kaart gebracht konden worden. Als onderdeel van de gevolgde *plan-do-check-act* cyclus bij de implementatie werden uiteindelijk de volgende interventies gebruikt: 1) Reorganisatie van het zorgproces waarbij niet langer de intaker, als lid van een apart intake-team, maar de behandelcoördinator van het behandelteam voor angststoornissen verantwoordelijk werd voor het opstellen van het behandelplan; 2) Het ontwikkelen en verspreiden van instructie materiaal voor hulpverleners en patiënten over de aanbevolen behandelingen volgens de richtlijnen; 3) Organisatie van instructiebijeenkomsten om de inhoud van de richtlijnen en de reikwijdte van de richtlijnaanbevelingen te bespreken; 4) Het trainen van professionals in relevante vaardigheden om de richtlijnen goed te kunnen toepassen; 5) Het routinematig vaststellen van de mate waarin aanbevolen interventies daadwerkelijk werden toegepast. Dit laatste als onderdeel van de behandelplanbesprekingen op het niveau van de individuele hulpverleners met de behandelcoördinator en ook als onderdeel van feedbacksessies met het hele behandelteam. Deze sessies vonden telkens plaats na enkele maanden om de gezamenlijk de voortgang van het project te evalueren en om nieuwe aandachtspunten voor het handelen te bepalen .

Op grond van de vergelijking van de resultaten van dossieronderzoek uitgevoerd bij 150 patiënten die werden behandeld binnen het angststoornissen team voor de start van de implementatie van de richtlijnen en 181 patiënten die werden behandeld binnen dit zelfde team na de start van de implementatie, werden significante verbeteringen vastgesteld bij het naleven van de belangrijkste kernaanbevelingen volgens de richtlijn, waarop een verbetering werd nagestreefd. Dit vormt een bewijs dat implementatie van richtlijnen in een behandelteam dat zich richt op patiënten met angststoornissen in een praktijksetting mogelijk is. Een stapsgewijze implementatie aanpak lijkt hierbij behulpzaam te zijn. Bij deze aanpak worden met op maat gemaakte interventies de specifieke knelpunten aangepakt.

In *hoofdstuk 3* wordt verslag gedaan van een beloopstudie waarin de uitkomsten van zorg vastgesteld werden van patiënten, die na de start van de implementatie van de angstrichtlijnen in Almelo voor de implementatie studie geïncludeerd werden. Doel van deze studie was na te gaan of het naleven van de richtlijnen superieure uitkomsten oplevert. Na 1 jaar werden daarvoor de behandelresultaten van 81 patiënten bij wie de richtlijnen correct waren nageleefd, vergeleken met die van 58 patiënten bij wie de richtlijnen ten onrechte niet waren nageleefd. Het bleek dat de bereikte klachtenreductie bij de categorie patiënten bij wie kon worden vastgesteld dat de belangrijkste, door de richtlijn voorgeschreven behandelstappen goed waren uitgevoerd, significant groter was in vergelijking met de categorie patiënten bij wie bij het zorgaanbod van de richtlijnen was afgeweken. Er werd tussen beide groepen patiënten geen significant verschil gevonden in verbeteringen in kwaliteit van leven. De groep patiënten waarbij de richtlijnen goed waren nageleefd, bleek wel meer tevreden te zijn over de gevolgde behandeling in vergelijking met de andere groep. Tevens was het aantal behandelcontacten geringer in de groep patiënten die correct volgens de richtlijnen behandeld werden. In de studie werd vastgesteld dat de richtlijnen bij 87% van de patiënten toepasbaar zouden zijn geweest. Het naleven van richtlijnen kan dus tot betere resultaten leiden en kan de zorg ook efficiënter maken. Tevens laat de studie zien dat de aanbevelingen uit de angstrichtlijnen breed toepasbaar zijn.

In *hoofdstuk 4* worden de resultaten van een studie gepresenteerd waarin het cohort patiënten uit Almelo, geïncludeerd na de start van de implementatie van de richtlijnen, vergeleken werd met een cohort patiënten dat werd behandeld binnen een vergelijkbare behandelsetting in Amsterdam alwaar de angstrichtlijnen alleen verspreid waren onder de daar werkende hulpverleners. De Amsterdamse patiënten waren geïncludeerd in de NESDA studie. Doel van deze vergelijkende studie was te bepalen of systematische implementatie van de angstrichtlijnen - zoals beschreven in hoofdstuk 2 - gepaard zou gaan met een betere adherentie aan deze richtlijnen en betere behandel resultaten, vergeleken met de situatie dat alleen passieve disseminatie van de richtlijnen plaatsvindt. Omdat in de NESDA studie alleen patiënten geïncludeerd werden die leden aan een primaire diagnose paniekstoornis met of zonder agorafobie, sociale fobie of gegeneraliseerde angststoornis, werden uit het Almelose cohort alleen deze patiënten geselecteerd voor de vergelijking. Na een jaar behandeling bleken de richtlijnen voor wat betreft de belangrijkste aanbevolen behandelstappen vaker nageleefd te worden bij patiënten behandeld binnen de

setting waar systematische implementatie van de richtlijnen plaatsvond (actieve conditie). Na een jaar lieten patiënten in de actieve conditie een significant sterkere daling zien op een vragenlijst voor het meten van angstklachten dan de patiënten in de controle conditie. Na twee jaar was dit significante verschil echter verdwenen, vermoedelijk omdat de patiënten uit de controle conditie vaker langer doorbehandeld werden. Er werd geen verschil tussen beide condities gevonden voor wat betreft de afname van comorbide depressieve klachten. Deze resultaten suggereren dat als richtlijnen beter worden toegepast er ruimte is voor verdere verbetering van de resultaten van de zorg. De conclusie is dat systematische implementatie van de angstrichtlijnen de kwaliteit van de zorg en mogelijk ook de efficiëntie ervan kan verbeteren.

In *hoofdstuk 5* worden de resultaten gepresenteerd van een studie waarin gekeken is naar de mogelijkheid om ongunstige uitkomsten van zorg te voorspellen bij de groep van 81 patiënten uit Almelo, waarbij vastgesteld kon worden dat de angstrichtlijnen goed waren nageleefd. Doel van het onderzoek was om vast te stellen of het mogelijk is te voorspellen welke patiënten met een angststoornis niet zullen reageren op een behandeling volgens de richtlijn en welke patiënten functionele beperkingen zullen blijven houden na 1 jaar behandeling, terwijl zij wel een behandeling volgens de richtlijnen hebben gehad. De voorspellende waarde van variabelen waarvan uit ander onderzoek bekend is dat ze de behandelprognose van patiënten met een angststoornis kunnen beïnvloeden werden in deze studie onderzocht. Voorbeelden van dergelijke variabelen zijn: leeftijd, geslacht, allochtone afkomst, opleidingsniveau, arbeidssituatie, inkomen, motivatie voor behandeling, aanwezigheid van motieven voor secundaire winst, de aanwezigheid van een comorbide depressieve stoornis, een comorbide angststoornis of een comorbide persoonlijkheidsproblemen en de mate van tevredenheid met de toegankelijkheid van de zorg. De stapsgewijze selectieprocedure voor het ontwikkelen van een predictie-model voor behandel nonrespons, leverde een model op met alleen geslacht en aanwezigheid van motieven voor secundaire ziektewinst als voorspellende variabelen. Mannen hadden een iets grotere kans op een behandel non-respons na 1 jaar en patiënten met een nevenmotief bij het zoeken van hulp verrassen genoeg een kleinere kans. De voorspellende waarde van dit predictie model voor behandel non-respons bleek echter zeer beperkt te zijn. De stapsgewijze selectieprocedure voor het ontwikkelen van een predictie model voor blijvende functionele beperkingen, leverde een model op met geslacht, de aanwezigheid van een comorbide angststoornis en tevredenheid met de toegankelijkheid van zorg als voorspellende

variabelen. Mannen leken een grotere kans op blijvende functionele beperking te hebben na 1 jaar en patiënten met een comorbide angststoornis een kleinere kans. Patiënten die ontevreden zijn met de toegankelijkheid van de zorg, hadden een grotere kans op blijvende functionele beperkingen. De mate waarin dit model met deze 3 voorspellende variabelen in staat lijkt onderscheid te maken tussen patiënten die een kleine dan wel grote kans lijken te hebben op blijvende functionele beperkingen na 1 jaar, blijkt op grond van de gevonden resultaten uitstekend. De conclusie moet voorlopig zijn dat het vooralsnog slecht mogelijk is te voorspellen welke cliënten onvoldoende van een behandeling volgens de richtlijnen zullen profiteren. Dit als gekeken wordt naar het optreden van behandelresponse als uitkomstmaat. Dit suggereert gelijktijdig dat met de huidige kennis er dus ook weinig reden is iemand met een angststoornis als primaire diagnose, een dergelijke behandeling te onthouden. Vanuit het perspectief van het voorkómen van langdurende invaliditeit lijkt daarbij als aangrijpingspunt voor de hulpverlening vooral rekening gehouden te moeten worden met eventueel ervaren problemen bij de toegankelijkheid van zorg. Het aanbieden van huisbezoeken of de inzet van E-health interventies zou in die voorkomende gevallen wellicht uitkomst kunnen bieden

In *hoofdstuk 6* worden de resultaten van verschillende deelstudies samengevat en besproken. Uit het huidige onderzoek kunnen moeilijk harde causale conclusies getrokken worden. Dat komt door het observationele karakter van de studies. Vervolgonderzoek naar de implementatie van de angstrichtlijnen zal opgezet moeten worden als een multicenter, cluster-gerandomiseerd, gecontroleerd experiment. Het lijkt voor de toekomst ook zinvol de toegevoegde waarde van het aanbieden van de opeenvolgende aanbevolen behandelstappen uit de richtlijn te onderzoeken. Idealiter zou er daarbij ook gekeken worden naar betere voorspellers van het behandelsucces, van de verschillende aanbevolen behandelstappen. Kennis hierover zou de doelmatigheid van zorg immers verder kunnen verbeteren.

In *hoofdstuk 7* wordt de Engelstalige samenvatting van dit proefschrift gegeven.

Dankwoord

Mensen die geen weet hebben van mijn interesse in de Japanse geschiedenis en dan vooral die van de Japanse krijgskunsten, zal de keuze voor een Japanse prent op de omslag wellicht verbazen. De anderen daarentegen zouden zich kunnen verwonderen over de keuze voor de specifieke prent van een karper die tegen een waterval opzwemt. Het is niettemin een weldoordachte keuze. De karper die tegen een waterval opzwemt wordt in Japan geassocieerd met moed, doorzettingsvermogen, wijsheid, geluk, en succes. Het is inmiddels mijn ervaring dat de implementatie van richtlijnen in de ggz, moed, doorzettingsvermogen, wijsheid en geluk vraagt om deze succesvol te laten zijn, hetgeen de zwemmende karper een passende metafoor maakt.

De genoemde kwaliteiten zijn evenzeer onontbeerlijk geweest bij mijn persoonlijke tocht van de afgelopen 10 jaar, waarvan deze dissertatie het eindpunt vormt. Ook daarom sprak het beeld op de omslag mij zo aan. Mijn enthousiasme voor mijn vak kende de afgelopen jaren nauwelijks grenzen. Eigenlijk ben ik na mijn afstuderen daarbij voortdurend nieuwe uitdagingen aangegaan, waaronder het combineren van hulpverleners- en onderzoekstaken, het volgen van diverse opleidingen en uiteindelijk ook het aanvaarden van de functie van hoofd van wetenschappelijk bureau bij HSK. De duur van dit promotietraject maakt tegelijkertijd duidelijk dat ik mij daarbij uiteindelijk ook wel behoorlijk heb verkeken op de hoeveelheid werk, die het aangaan van al deze uitdagingen met zich meebracht. Zeker waar het de observationele opzet van mijn promotie onderzoek betreft, deden zich de nodige uitdagingen voor waar het ging om het geplaatst krijgen van de artikelen waaruit dit proefschrift bestaat. Hierbij was het voor mij persoonlijk dan ook heel nadrukkelijk vaak een kwestie van tegen de stroom inzwemmen en flink doorzetten. Het beeld van de karper op de omslag is daarbij alleen misleidend in die zin dat deze karper toch wel erg alleen is in zijn tocht omhoog. Dit in tegenstelling tot de steun en hulp die van velen heb ontvangen bij het succesvol afronden van het proefschrift. Ik kan oprecht zeggen dat ik zonder de betrokkenheid van de meeste van deze personen zelfs helemaal nooit tot de afronding van dit promotieonderzoek gekomen zou zijn.

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weet dat ik enorm waardeer dat jullie geregeld uit jullie *comfortzone* traden door te proberen gedisciplineerd de angstrichtlijnen te volgen. Hoewel dit nergens expliciet in dit proefschrift beschreven staat weet ik dat voor sommigen de gunfactor naar mij toe daarbij een belangrijke motivatie was. Mijn dank aan deze hulpverleners uit Almelo is daarom extra groot. Ik hoop dat dit proefschrift in ieder geval duidelijk maakt dat jullie werk hierin niet onbeloond is gebleven getuige de positieve resultaten die het heeft opgeleverd!

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Marc Verbraak neemt als tweede promotor een extra bijzondere plaats in. Deels vanwege onze gedeelde professionele achtergrond maar vooral omdat mijn aspiraties voor dit specifieke promotietraject in de eerste plaats bij jou zijn begonnen. Beste Marc, als pas afgestudeerd psycholoog belde ik jou met de gewaagde boodschap dat alles wat jij in je werkende leven op dat moment deed, datgene was wat ik mijzelf uiteindelijk ook het liefste zag doen. Ik wilde ook zorgtaken, wetenschappelijk onderzoek en onderwijstaken combineren. Daarbij had ik ook nog de moed om te vragen of je me daarbij op weg kon helpen. Wat een geluk dat al mijn wensen wat dat betreft inmiddels voor het merendeel in vervulling zijn gegaan. Je hebt wat dat betreft veel meer gedaan dan me op weg helpen! Ik dank je voor je indrukwekkende werk bij de totstandkoming en de voltooiing van dit project, waarbij je bijdrage als behandelcoördinator bij ADAPT ook niet onvermeld mag blijven om met name de psychologen in het begin mee te krijgen in het werken in het spoor zoals beschreven in de richtlijnen. Dank voor al je vertrouwen in me! Ik kan me verheugen op de extra ruimte die de afronding van deze dissertatie gaat opleveren, om nieuwe initiatieven te starten vanuit mijn functie als hoofd van het wetenschappelijk bureau bij HSK. Ik hoop daarbij ook nog lang met je kunnen blijven samenwerken en van je te kunnen blijven leren.

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Curriculum Vitae

Maarten Kornelis van Dijk werd op 2 januari 1980 geboren in Groningen. De middelbare school volgde hij in Baarn bij de scholengemeenschap Het Baarnsch Lyceum, alwaar hij in 1998 zijn VWO-diploma behaalde. Na het afronden van de algemene gamma propedeuse bij de Universiteit van Utrecht, ging hij bij dezelfde universiteit Klinische en Gezondheidspsychologie studeren. Zijn doctoraal examen psychologie ronde hij uiteindelijk in 2003 af. Tijdens zijn studie psychologie deed hij zijn eerste ervaring met het werk in de geestelijke gezondheidszorg op. Eerst door vanaf 2000 met grote regelmaat als groepsleider in te vallen op diverse verblijfsafdelingen voor kinder en jeugdpychiatrie van zorginstelling Zonnehuizen, te Zeist. Later vanaf 2002 als invalkracht in de functie van helpende op verschillende klinische afdelingen voor volwassenen, binnen Altrecht.

Vanaf 2004 ging hij ook daadwerkelijk als psycholoog aan de slag binnen een ambulant team voor de behandeling van angststoornissen in Almelo, van het voormalige Adhesie, nu onderdeel van Dimence. Eind 2004 werd hem een subsidie van ZonMw toegekend en begon zijn promotietraject. Dit promotietraject werd gecombineerd met de opleiding tot Gezondheidspsycholoog, in het kader waarvan hij breder binnen Dimence werkervaring opdeed en waarbij hij in 2008 uiteindelijk zijn BIG-registratie als GZ-psycholoog behaalde. Hij volgde min of meer gelijktijdig ook de basis- en vervolgcursus EMDR. Ook ronde hij in 2009 met succes het cursorisch gedeelte van de Post-initiële Masteropleiding Epidemiologie van het EMGO af.

Vanaf januari 2010 werkt hij als hoofd van het wetenschappelijk bureau van HSK, waarbij hij onderzoek- en zorgtaken met elkaar blijft combineren. Zijn ervaring strekt vooral uit naar de behandeling van de zogenaamde 'common mental disorders'. Maarten verwacht na afronding van het bijbehorend opleidingstraject in de loop van dit jaar zijn registratie als cognitief-gedragstherapeut te behalen, zoals erkend door de Vereniging voor Gedragstherapie en Cognitieve therapie (VGCT). Per januari 2013 startte hij met de opleiding tot klinisch psycholoog, welke hij eind 2016 zal afronden.

Maarten woont samen en heeft twee zoons, 1 van 2 en 1 van 4 jaar oud.

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Appendice 1.
Process and treatment indicators

Table A. The definitive selection of process indicators for each disorder

Panic disorder	Percentage of patients with a panic disorder with co morbid severe depression and an indication for treatment with an antidepressant, who have been prescribed one of the antidepressants recommended in the guideline first of all
	Percentage of patients with a panic disorder with (moderately) severe agoraphobia with an indication for treatment with an antidepressant and who were prescribed one of the antidepressants recommended in the guideline first of all
	Percentage of patients with a panic disorder with an indication for treatment with an SSRI who have been prescribed an SSRI
	Percentage of patients with a panic disorder with an indication for treatment with a TCA, who have been prescribed a TCA
	Percentage of patients with a panic disorder with (moderately) severe agoraphobia with an indication for treatment with in vivo exposure, who have been offered in vivo exposure
	Percentage of patients with a panic disorder with (moderately) severe agoraphobia who have been offered in vivo exposure in combination with a pharmacotherapeutic treatment
	Percentage of patients with a panic disorder without (or with only mild) agoraphobia with an indication for treatment with panic-management training, who have been offered panic-management training
Social phobia	Percentage of patients with a social phobia of the generalized subtype with an indication for treatment with an SSRI, who have been prescribed an SSRI
	Percentage of patients with a social phobia of the generalized subtype with an indication for monotherapy with a benzodiazepine, who have been prescribed monotherapy with a benzodiazepine
	Percentage of patients with a social phobia of the specific subtype with an indication for treatment with a beta blocker, who have been prescribed a beta blocker
	Percentage of patients with a social phobia with an indication for treatment with in vivo exposure, who have been offered in vivo exposure
	Percentage of patients with a social phobia with an indication for cognitive therapy, who have been offered cognitive therapy
	Percentage of patients with a social phobia of the generalized subtype with an indication for following a social skills training, who have been offered a social skills training

Obsessive Compulsive Disorder	Percentage of patients with OCD with co morbid severe depression and an indication for treatment with an antidepressant, who have been prescribed one of the antidepressants recommended in the guideline first of all
	Percentage of patients with OCD with an indication for treatment with an SSRI, whom have been prescribed an SSRI
	Percentage of patients with OCD who did not respond to treatment with a second SSRI with an indication for treatment with an antipsychotic, whose treatment with an SSRI has been supplemented with an antipsychotic
	Percentage of patients with OCD with an indication for treatment with clomipramine, who have been prescribed clomipramine
	Percentage of patients with OCD with an indication for treatment with exposure and response prevention, who have been offered treatment with exposure and response prevention
	Percentage of patients with OCD with an indication for treatment with cognitive therapy, who have been offered cognitive therapy
GAD	Percentage of patients with a generalized anxiety disorder with an indication for treatment with paroxetine, who have been prescribed paroxetine
	Percentage of patients with a generalized anxiety disorder with an indication for treatment with venlafaxine, who have been prescribed venlafaxine
	Percentage of patients with a generalized anxiety disorder with an indication for treatment with buspiron, who have been prescribed buspiron
	Percentage of patients with a generalized anxiety disorder with an indication for treatment with cognitive therapy, who have been offered cognitive therapy
	Percentage of patients with a generalized anxiety disorder with an indication for treatment with exposure, who have been offered treatment with exposure
	Percentage of patients with a generalized anxiety disorder with an indication for treatment with applied relaxation, who have been offered applied relaxation
PTSD	Percentage of patients with PTSD with an indication for treatment with an SSRI, who have been offered an SSRI
	Percentage of patients with PTSD with an indication for treatment with a TCA, who have been offered a TCA
	Percentage of patients with PTSD with an indication for treatment with EMDR, who have been prescribed EMDR
	Percentage of patients with PTSD with an indication for treatment with imaginary exposure, who have been offered treatment with imaginary exposure
	Percentage of patients with PTSD with an indication for treatment with cognitive therapy, who have been offered cognitive therapy
Specific phobia	Percentage of patients with a specific phobia with an indication for treatment with exposure, who have been offered treatment with exposure
	Percentage of patients with a specific phobia with an indication for treatment with cognitive therapy, who have been offered cognitive therapy
Hypochondria	Percentage of patients with hypochondria with an indication for treatment with cognitive therapy, who have been offered cognitive therapy
	Percentage of patients with hypochondria with an indication for treatment with exposure and response prevention, who have been offered treatment with exposure and response prevention

Table B. Treatment indicators applicable when pharmacotherapeutic treatment is offered

Percentage of patients with an anxiety disorder who have been prescribed a certain type of medication (e.g. a TCA), where it has been decided to prescribe one of the medications recommended in the guideline (e.g. Clomipramine).
Percentage of patients with an anxiety disorder who have been treated with one of the recommended medications and who have been prescribed the medication according to the target dosage
Percentage of patients with an anxiety disorder who have been treated with one of the recommended medications and who had been prescribed the medication for the recommended number of weeks before the effects of the treatment were evaluated

Table C. Treatment indicators applicable when a form of exposure is offered

Percentage of patients with an anxiety disorder who have been offered a form of exposure, and who were given an explanation of the treatment before it began
Percentage of patients with an anxiety disorder to whom a form of exposure has been offered and who have been given exposure homework assignments on a consistent basis
Percentage of patients with an anxiety disorder who have been offered a form of exposure and in whom the effect of the treatment was evaluated after they had received it for the recommended number of weeks

Table D. Treatment indicators which are applicable when cognitive therapy is offered

Percentage of patients with an anxiety disorder who have been offered a form of cognitive therapy, and who were given an explanation of the treatment before it began
Percentage of patients with an anxiety disorder who have been offered a form of cognitive therapy and who have been given homework assignments associated with this therapy on a consistent basis
Percentage of patients with an anxiety disorder who have been offered a form of cognitive therapy, and in whom the effect of the treatment was evaluated after they had received it for the recommended number of weeks

Appendice 2.
Questionnaire relating to factors that impede or promote the application of the anxiety disorder guidelines

Instructions:

The following questionnaire is designed to look at your opinion about using the guideline. This is to determine whether in your view there are any particular problem areas, or whether you see using the guideline as an opportunity. This information will help to determine whether it is worthwhile considering introducing the guideline more widely and, if so, which particular points will require attention. Please tick the answer that corresponds most closely to your own situation and/or opinion.

1.	Do you have a copy of the guidelines?	☐ yes	☐ no			
2.	Do you have a summary of the guidelines?	☐ yes	☐ no			
		not at all	hardly	in part	most of it	all of it
3.	To what extent have you read the guidelines?	☐	☐	☐	☐	☐
		poor	limited	reason-able	good	very good
4.	How do you evaluate your own knowledge of the contents of the guidelines?	☐	☐	☐	☐	☐
		never	some-times	regularly	often	always
5.	How often do you currently use the guideline when treating patients?	☐	☐	☐	☐	☐
	I think that working according to the guidelines is:	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
6.	sensible	☐	☐	☐	☐	☐
7.	a good thing	☐	☐	☐	☐	☐
	To what extent do you agree with the following statements?	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
8.	I think that following the guide-lines would improve the quality of my work	☐	☐	☐	☐	☐

9.	My patients think that they should be treated according to the guidelines	☐	☐	☐	☐	☐
10.	I intend to (continue to) use the guidelines to treat the majority of my patients with an anxiety disorder	☐	☐	☐	☐	☐
11.	I am able to organize my work in such a way that I can apply these guidelines	☐	☐	☐	☐	☐
12.	I am able to maintain the chosen treatment approach over several successive treatment meetings with the patient	☐	☐	☐	☐	☐
13.	Others in my profession think that I should work according to the guideline	☐	☐	☐	☐	☐
14.	My aim is to try to (continue to) comply with the guidelines for the majority of the patients who I treat	☐	☐	☐	☐	☐
	To what extent do you agree with the following statements?	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
15.	I am able to apply the guidelines	☐	☐	☐	☐	☐
16.	Colleagues within my team think that I should work according to the guidelines	☐	☐	☐	☐	☐
17.	My superiors think that I should work according to the guidelines	☐	☐	☐	☐	☐
18.	I expect that I will (continue to) follow the recommendations in the guidelines for the majority of patients	☐	☐	☐	☐	☐
19.	It is difficult for me to adapt my normal working methods in order to use the guidelines	☐	☐	☐	☐	☐
20.	I think that in most cases, I will (continue to) use the guidelines	☐	☐	☐	☐	☐
21.	Following the guidelines makes the work of medical service providers more transparent, both for each other and for the outside world	☐	☐	☐	☐	☐
22.	Within the professional association which I have the most contact with, people think that patients should be treated according to the guidelines	☐	☐	☐	☐	☐

23.	Patients do not want to be treated according to the approach recommended in the guidelines	☐	☐	☐	☐	☐
24.	I will (continue to) design most of my treatment according to the recommendations in the guidelines	☐	☐	☐	☐	☐
25.	I expect that healthcare for patients with an anxiety disorder will improve through the use of the guidelines	☐	☐	☐	☐	☐

Original distribution of items:

- 5 items which indicate the extent to which professionals are familiar with the guidelines (1, 2, 3, 4, 5)
- 5 items which reflect the 'attitude' of professionals to working according to the guidelines (items 6, 7, 8, 21, 25)
- 5 items which give an impression of the 'social pressure' to use the guidelines experienced by professionals (items 9, 13, 16, 17, 22)
- 5 items which reflect a professional's assessment of their ability to adhere to the guidelines in terms of being able to control their own actions (items 11, 12, 15, 19, 23)
- 5 items which give an impression of a professional's actual intention to (continue to) use the guidelines (items 10, 14, 18, 20, 24)

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